~~DOES NOT CIRCULATE~~

Volume XIII APRIL 1952 Number 4

DISEASES OF THE NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

UNIVERSITY OF MICHIGAN
APR 28 1952
MEDICAL LIBRARY

CONTENTS:

THERAPEUTIC EFFECTS OF ACTH IN MYOTONIA DYSTROPHICA 99
Hans H. Reese and Henry A. Peters

EFFECT OF GLUTAMIC ACID ON CHRONIC PSYCHOTIC PATIENTS 106
Wendell J. Pile

PROBABILITY OF RELAPSE IN DEMENTIA PRAECOX 111
Lewis Danziger

PREGNANCY IN LOBOTOMIZED SCHIZOPHRENIA 116
W. G. Eliasberg

NEUROLOGICAL CLINICAL PATHOLOGICAL CONFERENCE 121

SANITARIA

ASSOCIATE EDITORS

A. E. Bennett, M.D.—Berkeley, California
Francis J. Braceland, M.D.—Rochester, Minn.
Franklin G. Ebaugh, M.D.—Denver, Colorado
Temple Fay, M.D.—Philadelphia, Pennsylvania
Milton H. Erickson, M.D.—Phoenix, Arizona
Hamilton Ford, M.D.—Galveston, Texas
Walter Freeman, M.D.—Washington, D.C.
George T. Harding, M.D.—Columbus, Ohio
A. Hauser, M.D.—Houston, Texas
Louis J. Karnosh, M.D.—Cleveland, Ohio
Frank H. Luton, M.D.—Nashville, Tennessee
Wm. Malamud, M.D.—Boston, Mass.
Karl A. Menninger, M.D.—Topeka, Kansas
Hans H. Reese, M.D.—Madison, Wisconsin
S. Bernard Wortis, M.D.—New York, N. Y.

Titus H. Harris, M.D.
Galveston, Texas
Editor-in-Chief

YEARLY SUBSCRIPTION $4.00
SINGLE COPIES 40 Cents
FOREIGN SUBSCRIPTION $4.50

George Bisgeir, B.S., LL.B.
Chicago, Illinois
Managing Editor

Founded 1879

RING SANATORIUM

Eight Miles from Boston at an Elevation of 400 feet

For the study, care and treatment of emotional, mental, personality, and habit disorders.

All recognized psychiatric therapies are used as indicated.

Cottage accommodations meet varied individual needs. Limited facilities for the continued care of progressive disorders requiring medical, psychiatric, or neurological supervision.

Consultants in all Specialties

BENJAMIN SIMON, M. D.
Director

CHARLES E. WHITE, M. D.
LOUIS BEENNER, M. D.
WILLIAM B. SHELTON, M. D.
Associates

ARLINGTON HEIGHTS, MASSACHUSETTS
Telephone AR 5-0081

FRANCIS W. RUSSELL
Executive Secretary

HARDING SANITARIUM

WORTHINGTON, OHIO

For Nervous and Mental Disorders

NINE MILES NORTH OF STATE HOUSE — COLUMBUS

GEORGE T. HARDING, M.D.
HARRISON S. EVANS, M.D.
Medical Directors

CHARLES L. ANDERSON, M.D.
Clinical Director

L. HAROLD CAVINESS, M.D.
CHARLES W. HARDING, M.D.
JOHN A. WHIELDON, M.D.
NELLIJA RUBENIS, M.D.
RAY M. KELLOGG, M.D.

TELEPHONE COLUMBUS FR. 2-5367

Compton Sanitarium

AND

Las Campanas Hospital

COMPTON, CALIFORNIA
(Near Los Angeles)

Compton Sanitarium is a private psychiatric hospital with 120 beds. Emphasis is given psychotherapy by a staff of resident psychiatrists. Other treatment procedures are duly evaluated and administered. Careful records are maintained. There are psychiatrically trained graduate nurses; student nurses through affiliation; nursing attendants; dietitian; occupational therapist; recreational therapist; hydrotherapist; masseuse. Las Campanas Hospital (43 beds) provides adjunct general hospital facilities. Compton Sanitarium and Las Campanas Hospital are approved by the American College of Surgeons.

G. CRESWELL BURNS, M.D., *Medical Director.*

BEVERLY HILLS CLINIC and SANITARIUM

For

The Study and Treatment of Nervous and Mental Diseases

218 N. WESTMORELAND — DALLAS 11, TEXAS

This sanitarium is a psychopathic hospital with a home-like environment and is equipped to treat psychiatric and neurological cases in a most scientific manner by means of psychotherapy, occupational therapy, recreational therapy, and physiotherapy, including insulin and electroshock treatment as well as psychosurgery. There is a trained psychologist as well as a trained social worker. An X-ray machine and an electroencephalograph are available.

ARTHUR J. SCHWENKENBERG, M.D.
Medical Director

JOHN C. POWELL, JR., M.D.
Associate Psychiatrist

CHRISTINE ALLOWAY, M.D.
GUY B. FAIN, M.D.
Resident Psychiatrists

JOSEPH L. KNAPP, M.D.
Associate Psychiatrist and Clinical Director

STEPHEN WEISZ, M.D.
ROBERT E. WINN, M.D.
Visiting Neuropsychiatrists

VOL. XIII APRIL 1952 No. 4

Published monthly by
PHYSICIANS POSTGRADUATE PRESS
277 Broadway, New York 7, New York

EDITORIAL OFFICES
UNIVERSITY OF TEXAS SCHOOL OF MEDICINE
800 Avenue B., Galveston, Texas

Entered as second-class matter at the Post Office at New York, N. Y.

DISEASES of the NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

Therapeutic Effects of ACTH in Myotonia Dystrophica

HANS H. REESE, M.D., and
HENRY A. PETERS, M.D.
Madison, Wisconsin

Myotonia dystrophica (MD) is recognized as a complex polyendocrine disorder. Distinct muscular dystrophies or atrophies with functional disabilities with myotonic after-contractions, capsular cataracts, testicular atrophy with impotency, premature alopecia characterize the symptomatology. These clinical findings point to a disturbance of the central hormonal control regulation in the hypothalamic-pituitary tropic region. A series of fifteen cases, 13 males, 2 females, of variously advanced myotonia dystrophica are reviewed. Seven males received a ten day course of intramuscular ACTH which was repeated in two patients, bringing the total response reactions and evaluations to nine cases. In every instance we compared the muscle charts, the slit lamp examinations to determine the degree of cataract, the biopsies of muscles and in two cases of testes. We studied urinary creatine and creatinine excretions in twenty-four hour specimens, basal metabolic rates, cholesterol, calcium-phosphorus ratios, potassium, blood levels, total and differential blood counts, electrocardiograms, and x-rays of the skull for pituitary estimations. Ergographic recordings of the flexor muscles of the right fingers as our muscular efficiency controls were repeatedly checked. The patients were evaluated constantly for the presence, subsidence or absence of the mechanical myotonic or myostatic reaction before, during and after treatment schedules. Diets consisted of the regular hospital food.

All studies were repeated during and after ACTH medication which was administered intramuscularly four times a day each in 25 milligram dosage. The cases were from moderate to advanced. Three of seven patients had no family history of this condition; however complete examination of the family members were not carried out, so that subclinical cataract formation or non-disabling muscular pareses with myotonic reactions could not be ruled out.

In all instances the metabolic rate was normal or reduced (—14 average) as were the cholesterol levels (274 average). These findings were not influenced by ACTH therapy. Muscle biopsies and testicular biopsies were considered typical (figures 1, 2, 3, 4, and 5). Blood counts, urinalyses, potassium, phosphorus, calcium, and albumin-globulin rations were essentially normal and not influenced by ACTH. Abnormal creatine excretion was present in all cases; it was modified under treatment in three cases on five separate occasions. Abnormal creatine excretion was recorded during and after treatment in the cases with negative urinary creatine values before treatment. Electrocardiographic findings in all cases were abnormal (revealing decreased amplitude of T waves, BB block and delayed I.V. conduction as the most frequent findings), but showed improvement consisting of increased amplitude of T-waves during ACTH treat-

From Department of Neurology and Psychiatry, Medical School, University of Wisconsin.

ment in three cases. X-rays of the skull were all negative with normal configurations of the sella turcica in size; in only two cases a moderate exostosis frontalis was present.

In all cases following inception of ACTH injections there was a marked feeling of well being. The nasal and dysarthric speech, so typical of the MD disease, became less pronounced, and the pronunciation on the whole was more articulate and the voice of greater volume. The patients walked more erect, many carried their food trays for the first time in many months. Myotonia elicited in tongue and thenar eminences by mechanical percussion disappeared after the third or fourth day of treatment in all but one case in which it was much reduced; however the myotonic phenomena returned two or three days following cessation of the treatment to a former level. Ergographic achievements, retested on the seventh to ninth day of treatment in all instances, revealed an increased ability to do manual work or to raise a set load a greater number of times without fatigue due to synergic relaxation in the muscular tonicity, amounting to fifty per cent increase over the pre-treatment level, but the total manual or grip strength measured by ergograph means remained stationary without ever reaching a normal level. We have evaluated the comparative efficiency of quinine sulfate and ACTH and have concluded that the performance record on the ergograph after quinine was only slightly, if at all improved in myotonia dystrophica, a distinct difference of our results obtained with ACTH.

Slit lamp examination revealed no change in the existing cataract formations before and after treatment, however, the time interval is too short to permit deductions if this lenticular finding can be arrested through repeated courses of ACTH therapy. Needless to say, a mature cataract already present should follow the ophthalmological criteria for surgery.

Of seven patients only one was of low intellectual endowment. All patients displayed a peculiar personality response reaction which included a disregard for the incapacity and in several instances a tendency to boast of their native endowment. This included a statement by one, that he was the fastest calculator that he knew of, though performance did not bear this out; another claimed to be one of the best soft shoe dancers. During ACTH therapy the affect was altered somewhat, and these patients became less demanding and seemingly better integrated in their behavior. It seems probable that the personality reaction is in most cases a compensatory mechanism.

Three of the patients were incapacitated from a vocational standpoint, the others were still gainfully employed, one as a bartender, another as a farmer, another as an attendant in a hospital colony. B.B. continued to do work on a relative's farm.

Discussion

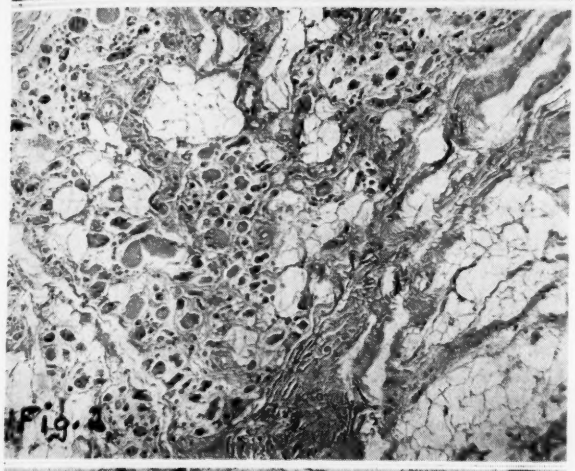
The pathological anatomy of myotonia dystrophica has been documented in an abundant literature. Suffice to name Erb[1] and Thomasen.[2]

Steiner,[3] Curshmann[4] and Naegele[5] called attention to the dominance of endocrine symptoms and signs, postulating a defect in the "central trophic organ." Curshmann and Naegele noted a tendency toward eosinophilia, anemia and polycythemia as hematopoetic findings of this "pluriglandular illness." We cannot support these statements from our blood studies. Lundborg[6] suggested a hypoparathyroid etiology in view of the frequent cataract formations. Our calcium, phosphorus and bone studies do not sustain the abnormal calcium metabolism theory. Goldzieher[7] referred to the similarity with Addison's disease, i.e. fatigue, hypotension, low blood sugar and sugar tolerance curves. No uniform data as to hypotension, hypoglycemia or abnormal sugar tolerance are recorded in our cases except a tendency to lower blood pressure levels.

Use of cortico adrenal extract has been tried unsuccessfully by Kolb, Harvey and Whitehill.[8] Thomasen[2] reported therapeutic results with desoxycorticosterone acetate with all patients showing increased strength of hand clasp and less fatigue. Hesser, Langworthy and Vest reported increased strength with testosterone proprionate which was not confirmed by Thomasen nor by us. The use of anterior pituitary preparations were used in cases by Kolb, Harvey

and Whitehill, and by Waring, Ravine and Walker[10] with some effect in one of three cases described by the latter.

Waring, Ravine and Walker however felt that subjective improvement resulted from adjunctive medications: amino acetic acid, ephinephrine, pilocarpine without objective evidence of clinical changes. Our experiences with adrenalin, pilocarpine and amino acids in the muscular dystrophies have been



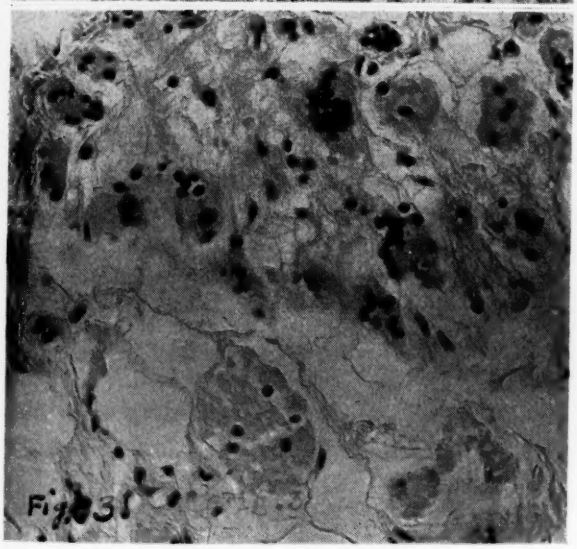
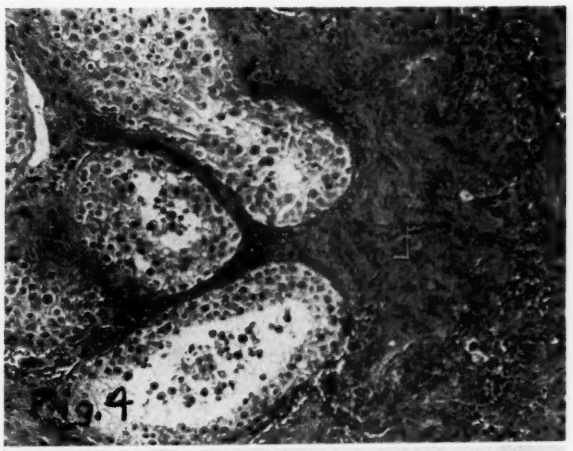


Figure 1. The longitudinal section of skeletal muscle from Case No. 4 contains muscle fibers in which granular and hyaline degeneration are seen. There is extensive increase of nuclei and linear arrangement of small pyknotic nuclei. Stain: hematoxylin and eosin. X 400.



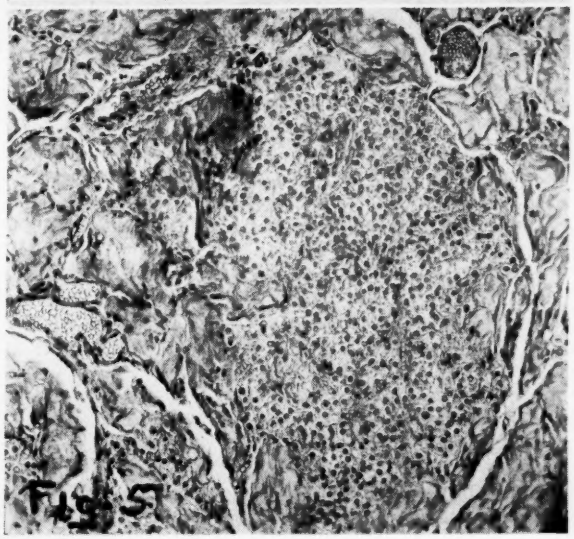


Figure 2. A transverse section of skeletal muscle from Case No. 1 in which the extenshive atrophy and necrosis of muscle fibers is seen, with considerable replacement by adipose tissue. Stain: hematoxylin and eosin. X 75.

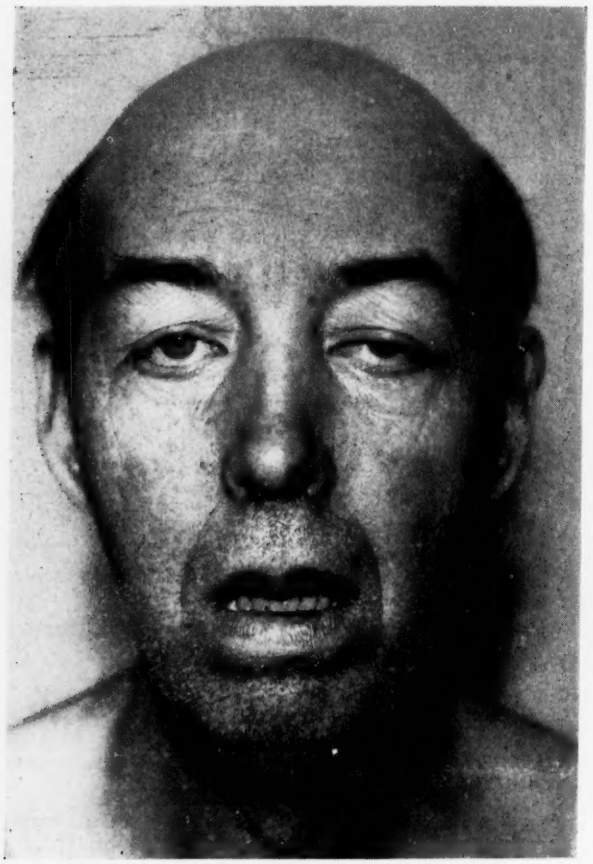
Figure 3. A higher magnification of tissue seen in Figure 2 permits discernment of the granular degeneration, the central location of nuclei within fibers, nuclear proliferation and increase in adipose tissue. Stain: hematoxylin and eosin. X 400.

Figure 4. A section of testis from Case No. 4 demonstrates the atrophy and sclerosis of many seminiferous tubules and the degenerative changes in the residual tubules. Stain: Masson trichrome. X 150.

Figure 5. In the section of testis from Case No. 5 the hyperplasia of Leydig or interstitial cells is conspicuous. The mass of cells is surrounded by completely atrophic and sclerotic tubules. Stain: Masson trichrome. X 150.

most discouraging. We have not resumed such additional measures with ACTH, but we have previously treated myotonic dystrophy with quinine and autonomic stimulating drugs (adrenaline and pilocarpine) without benefit.

Cortisone was tried in two cases of myotonia dystrophica by Shy, Brendler, Rabinovitch and McEachern[11] with relief from the myotonic reaction only while under treatment. More recently Shy and McEachern[12] reported analogous results with ACTH in three cases of myotonia dystrophica.



CASE I. Note alopecia with good beard and eye brow development, bilateral ptosis and typical myopathic facies.

Alopecia was present in all but one of our cases and was not associated with loss of body hair or beard growth. Cataract was present in all patients. Several of the reviewed cases were referred to our service by the Department of Ophthalmology, when a typical cataract formation suggested myotonic dystrophy. If cataracts occur in young persons—trauma, diabetes mellitus, tetany being excluded—they should be evaluated by the neurologist for myotonic dystrophy. The therapeutic effect of ACTH is promising in the initial phase and only then possibly able to arrest the endocrine dysharmony. Endocrine testicular atrophies suggest a defect in the hypothalamic—pituitary gonadal system. One patient had been capable of propagation (one child), though his divorced state precluded a study as to the transmission of the disease. Of the patients four were unmarried, two divorced and one married indicating probable early failure of sexual functions. In only one patient were the testes of almost normal size and consistency, however, the syndrome had developed only over a two year period. None of the patients displayed eunuchoid features indicating that failure of the testes had occurred after puberty. Seventeen ketesteroid determinations were not done.

Myotonia associated with myxedema has been reported. (Hoffmann syndrome.[13]) None of our patients had elevated basal metabolic rates, though in one case a basal metabolic rate of +19 in 1946 changed to —19 in 1951 at the time of present study with cholesterol levels at the upper limits of normal. Lowered basal metabolic rates are ascribed to the increased interstitial fibrosis and poor viability of the muscle tissues which causes low oxygen demand despite relatively increased body weight. In all but one case the blood pressure was in the low range; one exception revealed a mild hypertension and cardiac decompensation ten months after his first course of ACTH. All patients revealed evidence of myocardial involvement as evidenced by electrocardiographic charges.

Pathology

Pathologic changes in the adrenal cortex have been reported by Keschner and Davidson and others,[14] who described replacement of the fascicular layer and reticular layer of the cortex by a "peculiar reddish, avascular and somewhat edematous substance." The unaffected parts of the cortex contained lipoid substance, with much fibrosis and degeneration and falling out of the cells especially of the fascicular layer.

Examination of the pituitary gland and hypothalamus by Adie and Greenfield,[15] and

Weil and Keschner[16] revealed small cysts in the pars intermedia, while Bielschowsky, Mass and Ostertag[17] found increased numbers of more or less granulated, acidophilic cells with small nuclei and single hypertrophic principle cells. Keschner and Davidson[14] describe an increase in connective tissues with a diminution in the number of epithelial cells in the anterior lobe of the pituitary. The basophilic cells appeared unusually large with peripheral nuclei and the cells were distended with homogeneous basophilic substance. In the middle of the lobe the alveoli consisted almost entirely of eosinophile cells in various stages of degeneration, and in the anterior lobe was a considerable area of acellular connective tissue. There was a diffuse distribution of colloid in the acini, most marked in the posterior and lateral parts of the posterior lobe and pars intermedia. A pea-sized spongioblastoma was found originating in the corpus callosum and many of the ganglion cells of the paraventricular nuclei were swollen and disintegrated. There was scanty Nissl substance collected peripherally in the cells in addition to swollen, pale and eccentric nuclei. There were changes in the ganglion cells of the supraoptic nucleus and similar changes in the hypothalamus. Weil and Keschner[16] reported all degrees of change up to complete degeneration of the cells of the tuber cinereum and the supraoptic nucleus. Jager[18] in a recent study detected no changes in the adrenal glands, normal hypothalamic nuclei, an intact tuber cinereum, while the hypophysis showed an important increase in the number of basophile cells, and a considerable decrease in the number of eosinophile cells. A large cyst was found in the anterior lobe and scattered smaller cysts throughout the hypophysis. Jager concluded, that the main lesion must lie in the hypophysial portion of the hypophysio-hypothalamic system, and that symptoms of this condition (myotonia, muscular atrophy, and cataract) are probably a result of this lesion.

Case	Patient	Hospital number	When treated	No. of Courses
1.	W.H.K.	211287	11-28-50 and 12-28-50	2
2.	L.E.H.	274424	1-13-51	1
3.	A.F.U.	250320	5-17-51	1
4.	A.K.	154117	2-1-51 and 11-15-51	2
5.	B.E.B.	120830	3-20-51	1
6.	W.C.G.	279495	11-10-51	2
7.	R.A.T.	280245	1-13-52	1
				9

Two clinical reports will illustrate our problems and investigations in myotonia dystrophica.

Case 4. A.K. (Hospital No. 154117) age 43, unmarried schoolteacher of Swedish ancestry, had noted progressive stiffness and weakness of the hands, forearms and lower legs over the past seven to eight years. Accompanying the motor symptoms had been progressive testicular atrophy and loss of libido, increased balding and decreased vision. Following scarlet fever he had acquired a right ptosis; examination revealed a partial third nerve paralysis and enophthalmos. Right mastoidectomy in 1948. The father had, in his late years, a chorea-like picture; the grandfather had been an alcoholic. The patient and a brother have a marked exostosis of both elbows and chronic generalized ichtyosis.

Patient is overweight. I.Q. evaluation (Wechsler-Bellevue) placed him in the bright normal range. He has the typical myopathic facies with marked atrophy of the facial and especially of the sternocleidomastoid musculature. It is difficult to raise his head forward without manual assistance. Slit lamp evaluation revealed lens changes O.U. with minimal cataract formation of myotonia dystrophica type. Speech is typically nasal and articulation is "muffled." There is balding, the testes are atrophic. A poker spine reflected the x-ray diagnosis of rheumatic arthritis of the von Bechterew type. The muscle volume is reduced distally in both the upper and the lower extremities with a slapping gait due to bilateral foot-drop. There is marked weakness of the hand grasp, the typical mechanical myotonic reaction can be elicited by mechanical percussion of the thenar eminence and of the tongue. The blood pressure showed occasional elevated distolic pressure above 100 (e.g. 150/104); the heart tones are irregular and distant. Electrocardiograms taken over a three year period showed increased frequency of nodal premature contractions and progressively decreasing voltage.

Skull X-ray: Hyperostosis frontalis. Biopsy of the gastrocnemius muscle: breaking up of individual muscle fibers, decreased size of many fibers, the sarcolemma nuclei are increased in number.

Testicular Biopsy: considerable atrophy and sclerosis with some of the tubules still showing spermatogenesis; the Leydig cells are reduced by about fifty percent. Trace of albumin in the urine but fair ability to concentrate. The basal metabolic rate is within normal limits as is the cholesterol level. Albumin-globulin ratio revealed a shift with globulin of 3.0 and albumin of 3.3 milligrams. On present and previous admission abnormal urinary creatine excretion in each twenty-four hour urine.

Following and during ACTH therapy the patient was more alert and strength of his handclasps was increased. The myotonic after contraction became greatly reduced and the ergographic achievements improved by fifty percent. Creatine excretion ceased.

Electrocardiogram: Slowed rate, fewer premature contractions and decreased QRS time, increased voltage. However, two to three days after the therapy was terminated, the patient regressed to his former clinical status. In November 1951 the patient was admitted in a state of myocardial failure complicated by auricular flutter which is nine months after the ACTH therapy. He responded to digitalization and ammonium chloride. The following month the patient was again given a course of ACTH. An identical response was noted which included the cessation of urinary creatine excretion again and somewhat better performance on the ergograph.

Case 5. B.F.B., Hospital number 129830, age 51, a white male developed progressive wasting of the muscles with motor weakness in 1935 at age 34, and had been observed by us for six years. Accompanying the motor weakness was progressive atrophy of the testes and impairment of vision due to bilateral cataract of the M.D. type. Past medical history included possible rheumatic fever at age 16 and a cerebral contusion in 1945 for which he was hospitalized. He is divorced, with no pregnancies while married and in recent years loss of libido and potency. A sister, a brother and three paternal cousins had a similar muscular weakness.

Patient seems poorly nourished with a dorsal kyphosis, bilateral ptosis and atrophy of the facial muscles result in lack of expression and in the sphinx facies so typical of the condition. This was the only case without alopecia. On rising from the prone position he has great difficulty raising his head from the pillow due to almost complete atrophy of the sternocleidomastoid muscles. In addition there is atrophy with weakness of all distal muscle groups particularly the intrinic hand musculature and the lower legs with bilateral footdrop. Palpation of the muscles gives a peculiarly firm doughy consistency. He cannot clench his fist. On closing his hands as firmly as possible there is a delay of five to eighteen seconds before he can unclasp them. Mechanical percussion of the thenar eminences produced an adductor response which he cannot terminate voluntarily for more than ten to fifteen seconds. Percussion of the marginal tongue produced a marked dimpling present for ten seconds. Cataract was present O.U.

Urinalysis and blood count are normal. Blood potassium 20, cholesterol 331 with a basal metabolic rate of —3 and —4. Blood phosphorus 2.8 and calcium 10.8 milligrams percent. Wassermann, blood sugar and non-protein nitrogen normal. Sedimentation rate 13 millimeters. Cerebrospinal fluid negative. Glucose tolerance normal. Twenty-four hour urine specimens: creatine of 1.6 milligrams excretion. Total serum protein 5.9 milligrams, albumin to globulin 4.4 to 1.5.

Electrocardiogram: Advanced myocardial changes with first stage AV block and BB block.

Muscle Biopsy: Compatible with myotonia dystrophica showing increased nuclear prolifereation, atrophy of muscle fibers over scattered areas with fat replacement. *Testicular biopsy:* before treatment: complete atrophy of tubules with sclerosis and increased interstitial cells. The Leydig cells are increased in adenomatous clumps.

Previous therapy included glycine, quinine, and Testosterone with no objective or subjective improvement though the myotonic after contractions were reduced under Quinine.

Ergographic studies after quinine treatment showed a slight improvement over his earlier record. Following and during ACTH treatment a marked reduction of the myotonia was evident. Ergographic recording demonstrated an increased ability to do work amounting to two or three times the pretreatment level. Thorne count on the second day of ACTH therapy revealed 38 eosinophiles per c.c. as compared to a level of 205 eosinophiles without ACTH. The electrocardiogram showed slight increase in amplitude T waves. Creatine excretions were negative for the first time toward the end of the treatment and persisted negative five days after the treatment. Three days post treatment the signs and symptoms returned as previously. He is unable to carry on work as a janitor, but is able to do light farm work for compensation.

Discussion

Whether treatment with ACTH was responsible for the cardiac decompensation that resulted in one case (A.K.) cannot be ascertained. The phosphocreatine reserves could be depleted since in cardiac failure the heart muscle is also deficient in creatine. Suffice to say that A.K.'s electrocardiogram had shown progressive myocardial damage in the years under observation and that in contrast to the other patients, this patient had on occasion elevation of diastolic pressure (150/104).

Another case (No. 6, W.C.G.) developed a toxic psychosis three days after cessation of ACTH. He had been treated despite previous alcoholism and with marked hepatomegaly and evidence of hepatic dysfunction. In the past several episodes of esophageal bleeding had been present. A toxic psychosis might well have been conditioned by these factors rather than as the result of the therapy.

We conclude that the therapeutic results, though transient, support the hypothesis that myotonia dystrophica is fundamentally an endocrine deficiency primarily in the hy-

pophyseal-hypothalamic regulation center and secondly in the various endocrine glands, and that ACTH replaces the lacking tropic stimulation hormones at least in part. The muscle metabolism in three cases on five separate occasions showed termination of urinary creatine excretion for the first time thus halting probable phosphorcreatine depletion.

We recommend the treatment with ACTH for myotonic dystrophy, since no other form of treatment has shown alteration in the clinical status of this disorder. Our cases were not of recent inception and the endocrine dysharmonic process had produced an advanced clinical constellation. Whether treatment with ACTH and Cortisone will arrest the process, when the disorder is treated in the incipient stage and with repeated courses until a maintenance treatment is worked out, can only be answered after continuous studies. Biochemical substances such as glycine, glutamic acid, sodium succinate, and wheat germ oil are under observation in conjunction with ACTH therapy. Will prolonged or repeated courses with ACTH therapy produce a more rapid decompensation of the already failing primary central and subsequently of the peripheral endocrine system, or can the dysharmony be restored with clinical improvement? We are unable to answer these questions at the present time.

Conclusion

Clinical observations of seven patients with myotonia dystrophica treated with ACTH twelve months later have shown no evidence of a precipitous or progressive disability; the disorder, however, is not markedly improved though some patients have remained at limited work.

Authors' Note: We acknowledge with our thanks the assistance of Dr. John W. Harman, Department of Pathology, University of Wisconsin, who interpreted the pathologic specimens.

REFERENCES

1. Erb, W. H.: Die Thomsen'sche Krankheit, Leipzig, *F. C. W. Vogel,* 1886.
2. Thomasen, E.: *Myotonia,* a text. Publisher, *Aarhus* 1948.
3. Steinert, H.: Über des klinische und anatomische Bild des Muskelschwunds der Myotoniker. *Deutsche Zeitschrift für Nervenheilkunde* 37: 58: 1909.
4. Curshmann, H.: Über familiäre atrophische Myotonie, *Deutsche Zeitschrift f. Nervenh.* 45: 161, 1912.
5. Naegeli: Über myotonia atrophica, speziell über die Symptome und die Pathogenese der Krankheit nach 22 Fällen. *München Med. Wochenschrift* 64, 1631, 1917.
6. Lundborg, H.: Spielen die glandulae parathyreoideas in der menschlichen Pathologie eine Rolle? *Deutsche Ztschr. f. Nervenh.* 27:217, 1904.
7. Goldzieher, M. A.: Chronic Adrenal Insufficiency. *The Endocrine Glands,* New York-London 1939.
8. Kolb, L. C., and Harvey, A. M., Whitehill, M. R.: Mytonic Dystrophy and Myotonia Congenita with Special References of the Therapeutic Effect of Quinine. *Bull. John Hopkins Hospital,* 62:188, 1938.
9. Hesser, F. H., Langworthy, O. R., and Vest, S. A.: Muscle Strength in Myotonia Atrophica Improved by Testosterone Proprionate. *Endocrinology.* 26:241, 1030.
10. Waring, J. J., Ravine, A., and Walker, C. E.: Studies in Dystrophia Myotonica, *Arch. of Internal Medicine* 65, 763, April 1940.
11. Shy, G. M., Brendler, S., Rabinovitch, R., and McEachern, D.: Effects of Cortisone in Neuromuscular Disorders, Journal?, 144 no. 16 1353, 1951.
12. Shy, G. Milton and McEachern, Donald: Further Studies for the Effects of Cortisone and ACTH on neurological Disorders, *Brain,* 74: 354-362, 1951.
13. Hoffman, J.: Weitere Beitrag Zur Lehre von der Tetanie. *Deutsche Ztschr. f. Nervenh.* 9:278, 1897.
14. Keschner, M., and Davidson, C.: Dystrophia Myotonica, *Arch. of Neurol. and Psychiat.* 30, No. 6, December 1933.
15. Adie, W. J., and Greenfield, J. G.: Dystrophia Myotonica, *Brain,* 46, 73, 1923.
16. Weil, A., and Keschner, M.: Ein Beitrag zur Klinik und Pathologie der Dystrophia myotonica, *Zeitschrift für d. ges. Neurol. u. Psychiatrie,* 108: 687, 1927.
17. Bielschowsky, M., Mass, O., and Ostertag, B.: Über dystrophia myotonica; Volume Jubilare, *G. Marinesco,* 1933.
18. Jager, W. A. den Hartog: Clinical and Pathological Findings in a Case of Dystrophia Myotonica. *Arch. Neurol. and Psychiat.* 66: 178-190, August 1951.

Effect of Glutamic Acid on Chronic Psychotic Patients

WENDELL J. PILE, M.D.
Williamsburg, Virginia

It was noted by Weil-Malherbe[1] that 1(+)-glutamic acid is the only amino acid metabolized by the brain. Nachmanson and his associates[2] have found that 1(+)-glutamic acid has a catalysing effect on the rate of production of choline acetylase. Nachmanson and associates[3] also showed that choline acetylase, an enzyme, synthesizes acetylcholine. They further demonstrated[4] that electrical charges during nerve activity is connected with the release of acetylcholine. The above experiments seem to indicate that 1(+)-glutamic acid is related in some manner to cerebral metabolism.

The work of Price, Waelsch and Putman[5] who used d1-glutamic acid hydrochloride as an adjuvant in the treatment of petit mal seizures, was a report showing an increase of mental and physical alertness in the patients so treated. On this basis Zimmerman and Ross[6] investigated the effects of glutamic acid and its derivatives on the learning ability of the white rat. In this controlled study they found that "rats fed 1-glutamic acid learned the maze in fewer trials and in a shorter time than did the control rats."

These experiments on the simple maze "also suggested to Albert and Warden[7] the possibility that adding 1(+)-glutamic acid to the normal diet might enable white rats to learn more complex problems as well." Using the problem box[8] they found that supplementing the normal diet with 1(+)-glutamic acid caused white rats to advance further in a series of increasingly difficult problems.

Zimmerman and his group[9] next investigated the effect of 1(+)-glutamic acid in human subjects. They felt that glutamic acid did "have a genuine facilitating effect on mental functioning in human subjects." Zimmerman and associates[10] then determined the effect of glutamic acid on the intelligence of patients with mongolism and concluded that ". . . a positive trend is definitely indicated, suggesting that glutamic acid facilitates mental functioning in this form of mental deficiency also . . ."

Waelsch and Price[11] used glutamic acid as therapy in epilepsy. They found it not only ineffective in the treatment of grand mal epilepsy, but even noted that seizures may be increased in number. However, they did find that petit mal attacks were less in number and severity after glutamic acid therapy of 14 to 28 gms. daily was instituted. They noted an improvement in morale of this latter group. They noted further that there was no "evidence of any effect on the personality or the emotional stability."

However, Albert, Hoch, and Waelsch[12] in using glutamic acid on mental defectives observed that their patients behaved in a manner which ". . . suggested an improved emotional regulation." They felt ". . . that the performance of the total personality, rather than of some circumscribed intellectual functions, showed improvement." They also administered 10 to 30 cc of a 10 percent solution of glutamic acid intravenously to patients who had just received electric shock treatment and were at the height of their confusional state. They gained the impression that administration of glutamic acid shortened the periods of confusions and memory impairment. They also felt that emotional imbalance as noted sometimes after electric shock treatment improved first—". . . and the change in behavior for the better preceded the improvement in the intellectual performance." They felt it might be possible that glutamic acid—"does not so much influence or increase the intellectual ability as such, but only enables the patient to regain his intellectual function which was inhibited by other mechanisms." If this latter premise were true, it might be argued that intellectual functions—which are certainly inhibited by psychoses that contribute to emotional imbalance—may be regained through improving the emotional balance and the psychosis by the administration of glutamic acid.

From Eastern State Hospital, Williamsburg, Virginia.

There seem to have been no studies done using glutamic acid on psychotic patients; specifically patients with the diagnosis psychosis with mental deficiency. It was also felt that dementia praecox patients, hebephrenics specifically, who in deterioration resemble closely the mental defective psychotics might possibly show a change in their personality, symptoms and affect. Especially was this considered when it was realized the importance of glutamic acid in brain metabolism. There also seems to be a growing appreciation of the importance of possible disorders of brain metabolism in the onset of dementia praecox.[13]

This present study was conceived in the belief that the next logical step in the use of glutamic acid should be its trial on certain psychotic patients. To begin with, a one month's trial of 12 gms. of glutamic acid was given daily to a female patient who presented symptoms of psychosis with mental deficiency and dementia praecox, hebephrenic type. Several neutral observers observed that she became more sociable and alert, with an improvement of the personality.

Somewhat encouraged by this promising result, the writer set forth a plan for research as follows:

1) Twenty patients were chosen from the female service.

2) Ten patients with a diagnosis psychosis with mental deficiency; eight cases with dementia praecox, hebephrenic type; and two cases with dementia praecox, catatonic type—extreme deterioration—were selected for this study. The patients ranged in age from 15 to 45 years with an average of 30.85 years. All in the group were considered chronically ill.

3) Five patients classified as phychosis with mental deficiency, four dementia praecox, hebephrenic type, and one dementia praecox, catatonic type, extreme deterioration, received glutamic acid daily for six months.

5) Prior to treatment, each patient was examined by three psychiatrists; individual background, personality, and psychotic symptoms were noted.

6) Prior to treatment each patient was given a Stanford-Binet Intelligence test, Form L.[11]

7) The patients were started on a total of 12 gms. daily of glutamic acid given in divided doses three times daily. No signs of illness or reaction to the drug was noted and after one month the dosage was doubled to 24 gms. daily given in three divided doses. Again no drug reactions were noted. Several patients receiving glutamic acid "complained" of increased appetite. Several patients receiving the placebo had the same "complaint." The patients were maintained on this dosage for the final five months of the study.

In reviewing the studies of Zimmerman[10] it is noted he used a sliding scale dosage plan. His average doses varied from 15 to 30 gms. daily in most cases. In this present study it was difficult to plan a dosage plan for the individual patient owing to the extremely poor contact they had with reality. It may well be, particularly with reference to the demential praecox patients, that they had increased tolerance to glutamic acid. The increased tolerance to other substances, specifically hormones, has been noted by Hoskins.[15]

8) Following six months treatment, each patient was given the Stanford-Binet intelligence test, Form M being used instead of the Form L that was given prior to treatment.

9) After the complete treatment, the patients were again examined by the three psychiatrists to determine any personality change or any change in psychotic symptoms.

10) A weight chart was kept to see if there was any correlation between changing weight and changing psychotic symptoms.

For convenience the patients were placed in one ward. They could be observed more readily and it would be easier to give them the drug. A ward was chosen where the majority of the selected group had resided, it being felt that the external surroundings should be changed as little as possible. The few outside patients were moved to this ward. However, since they were all formerly on chronic wards, the change probably had little effect on their mental symptoms. A capable charge attendant was chosen who

FIG. 1
EXPERIMENTAL GROUP

Patient	Diagnosis	Age in Years	Hospital tenure in years	STANFORD-BINET in Months Achieved: Before Glutamic Acid Form L	After Glutamic Acid Form M	Net change	Weights in Pounds: Before Glutamic Acid	After Glutamic Acid	Net change	Clinical evaluation after Glumatic Acid
M.J.	d.p. e. Catatonia	39	6	72	76	+ 4	116	117	+1	Psychotic symptoms much increased. Pt. much more untidy (—)
C.B.	Psychosis with Mental Deficiency	24	3	38	43	+ 5	95½	104	7½	(0)
M.H.	P. with M.D.	37	5	48	54	+ 6	120	113½	—6½	(+) Psychotic symptoms decreased. More accentive.
D.L.	d.p. hebephrenia	25	9	88			discharge at 5 mos. of treatment			(+) More active More alert
M.E.	d.p. H.	20	4	24*	12	—12	133	135	+2	(0)
M.B.	d.p. H.	27	6	9*	5	— 4	101	98	—3	(0)
C.C.	d.p. H.	26	5	81	106	+25	87½	96½	+9	(0)
M.R.	d.p. H.	26	10	27*	24*	— 3	99	125	26	(0)
M.A.A.	d.p. H.	15	1	98	116	+18	112	113	+1	(0)
A.R.B.	p. with M.D.	45	27	14*	8	— 6	126	122	—4	(0)
Average		28.2	7.6	Mean increase in months		+3.4	Mean increase in Weight		+3.77	

FIG. 2
CONTROL GROUP

Patient	Diagnosis	Age in Years	Hospital tenure in years	Before Placebo Form L	After Placebo Form M	Net change	Before Placebo	After Placebo	Net change	Clinical evaluation after Placebo
V.J.	Psychosis with Mental Deficiency	28	6	82	96	+14	135	135½	½	0
L.B.	Psychosis with Mental Deficiency	36	11	52	60	+ 8	92½	95	2½	0
S.C.	Psychosis with Mental Deficiency	37	4	122	142	+20	166	173	7	(+) Alert — pleasant
E.S.	D.P.C.	37	5	2*	2*	0	107	111	4	0
M.H.	D.P.H.	25	4	130	136	+ 6	106½	109	2½	(+) Well oriented — No psychotic symptoms Still, child-like
M.S.	Psychosis with Mental Deficiency	42	1	68	Discharged					Improved after 4 Mos.
L.Y.	Psychosis with Mental Deficiency	33	18	1*	3*	+ 2	116	115½	—½	0
V.H.	Psychosis with Mental Deficiency	30	2	132	128	— 4	111	113½	2½	+ More attentive Responses
A.L.C.	D.P.H.	37	17	60	72	+12	108	108	0	+
D.A.B.	D.P.H.	28	3	88	112	+24	118½	118	—½	0
Average		33.3	7.1	Mean increase in months passed		9.1	Mean increase in Weight Average		1.88	

*Cases are those on whom no basal age was obtained on either or both tests. In these cases only the number of months actually passed on each test was used. Hence these figures bear no relationship to the mental age of the patient.

was warned not to show particular attention toward any one patient in either the experimental or the control group.

It was felt that to determine the clinical progress of the patients, the originator of the project (and the only one besides the attendant who knew who received glutamic acid and who received the placebos) would be motivated unconsciously to favor the group receiving glutamic acid. For this reason three psychiatrists, who were unaware as to which drug the patient were receiving, kindly volunteered to check the clinical progress of the patients. The patients were seen by the above observers a day or two prior to the beginning of the study. The history of each patient was read. Additional facts as to personality, ward behavior and sociability were added by attendants who knew the patients by their daily and constant contact. Complete memoranda were kept by each of the three psychiatrists. It was decided there should be as little contact with the patients as possible by the psychiatrists during the study. Occupational therapy cooperated by keeping their therapy at a minimum and by giving no one of the group special attention. At the conclusion of the six month period, the three examiners again interviewed the patients. The cases were reviewed by the examiners; individual notes and changes in the patients' psychotic condition and personality were noted. The opinion of each examiner was tabulated independently of the others. No change was marked "O." Improvement of psychotic symptoms of personality was marked "+." Exacerbation of psychotic symptoms or a change for the worse in the personality was mark "—." Of course the type and a description of the change, if any, were recorded. In each case at least two and often all three of the examiners agreed as to the change or lack of change to be noticed in the patients.

The psychologists cooperated by testing immediately before the therapy was begun and also immediately after the therapy was terminated.

The charts, figures 1 and 2, show the results of the six months study. Of the experimental group, the clinical improvement, where noted, was accompanied by a slight increase in the number of months achieved on the Stanford-Binet tests.[3,4] Of the control group the one outstanding example of clinical improvement, accompanied by an increase of twenty months passed on the Stanford-Binet test, was a patient who while diagnosed psychosis with mental deficiency, had a typical psychotic picture of manic depressive psychosis. The other patients' psychoses resembled that of the dementia praecox classification. It undoubtedly is correct that this patient was depressed when she was first tested; and during the ensuing six months she gradually attained a more even keel. She also showed the greatest weight gain of any in the control group—7 pounds. The mean increase of months achieved on the Stanford-Binet tests in the control group was 9.1.

Workers in the past have commented on the frequently observed phenomenon of an increase in weight in a patient being accompanied by an improvement in the psychotic picture. Bellak[16] noted that "some successfully treated patients show a gain in weight," and felt that it might be due to "increased metabolism." Baganz and Norris[17] noted a "concomitant increase in weight following pharmacological shock therapy for schizophrenia." While the experimental group showed a slightly higher than average gain in weight—(3.77 pounds)—there was no correlation between gain in weight and the clinically observed improvement. In fact, in one case (M.D.) of improvement noted there was a weight loss of 6½ pounds. In the control group there was a slight increase in weight accompanying the clinically observed mental improvement.

It is to be noted there are changes in the number of months passed as seen on the Stanford-Binet test that are excessive as regards gain or loss.

It must be remembered that in dealing with psychotic patients, the factors of empathy, rapport, and individual idiosyncrasies, that only those who are psychotic possess play a part in the test results. It also should be mentioned that different psychologists did the testing prior to the patients receiving the drugs and after the conclusion of the experiment due to circumstances beyond our control. Patients respond differently to different people. The results may

have been altered by that factor. Since the difference in the improvement of intelligence between the experimental group and the control group in this study favored the control group, some may wish to say that this study furnishes proof that the findings of Zimmerman, Waelsch, et al., are negated. For the above mentioned reasons this writer feels that this study does not negate the findings of these workers. This study has shown actually that in controlled circumstances 24 gms. of glutamic acid given daily for six months to a group of chronically psychotic patients does not improve or alter substantially the psychotic symptoms, personality or the intelligence quotient of the patients tested.

It must be added that the clinical evaluations that were made by the psychiatrists were necessarily unbiased. In such subjective experimental work it is important that the possible partiality and bias of the research originator be kept at a minimum.

Conclusion:

A group of twenty psychotic patients with diagnoses psychosis with mental deficiency, dementia praecox, hebephrenic type, and dementia praecox, catatonic type, with gross deterioration, were chosen for this study. Ten received glutamic acid (24 gms. daily) for six months. Ten received placebos for six months. Psychological determinations and clinical determinations seemed to show that glutamic acid was ineffective in the classification chosen for study.

Author's Note: The glutamic acid used in this research was supplied by Parke, Davis & Company, Detroit, Michigan.

The author acknowledges with his thanks the aid and cooperation given by G. L. Jones, M.D., E. Beamer-Maxwell, M.D., and R. A. Mora, M.D., for their cooperation in determining the clinical results, and the aid and cooperation of E. Williams and L. Terrill for conducting the testing and tabulating the results.

BIBLIOGRAPHY

1. Weil-Malherbe, H.: Studies on Brain Metabolism: Mechanism of Glutamic Acid in Brain, *Biochem. J.* 30:665, 1936.
2. Nachmanson, D., John, H. M., and Waelsch, H.: Effect of Glutamic Acid on the Formation of Acetylcholine, *J. Biol. Chem.* 150:485, 1943.
3. Nachmanson, R., and Machado, A. L.: The Formation of Acetylcholine: A New Enzyme: Choline Acetylase, *J. Neurophysiol.* 6:397, 1943.
4. Nachmanson, D., Cox, R. T., Coates, C. W., and Machado, A. L.: Action Potential and Enzyme Activity in the Electric Organ of Electrophorous Electricus: II. Phosphocreatine as Energy Source of the Action Potential, *J. Neurophysiol.* 6:383, 1943.
5. Price, J. C., Waelsch, H, and Putman, T. J.: d1-Glutamic Acid Hydrochloride in the Treatment of Petit Mal and Psychomotor Seizures, *J.A.M.A.* 122:1153, 1943.
6. Zimmerman, F. T., and Ross, S.: Effect of Glutamic Acid and Other Amino Acids on Maze Learning in the White Rat, *Arch. Neur. and Psychiat.* 51:446, 1944.
7. Albert, K. E., and Warden, C. J.: The Level of Performance, the White Rat, *Science* 100:476, 1944.
8. Warden, C. J., Jenkins, T. N., and Warner, L. H.: Comparative Psychology, New York, the *Ronald Press Co.*, 1935, vol. 1,350.
9. Zimmerman, F. T., Burgmeister, B. B., and Putman, T. J.: Effect of Glutamic Acid on Mental Functioning in Children and in Adolescents, *Arch. Neur. & Psychiat.* 56:489, 1946.
10. Zimmerman, F. T., Burgmeister, B. B., and Putnam, T. J.: Effect of Glutamic Acid on the Intelligence of Patients with Mongolism, *Arch. Neur. & Psychiat.*, 61:275,1949.
11. Waelsch, H., and Price, J. C.: Biochemiol Aspects of Glutamic Acid Therapy for Epilepsy, *Arch. Neur. & Psychiat.* 51:393, 1944.
12. Albert, K., Hoch, P., and Walesch, H.: Preliminary Report on the Effect of Glutamic acid Administration in Mentally Retarded Subjects, *Jr. of Nerv. & Ment. Diseases* 104:263, 1946.
13. Jones, G. L.: Supt. Eastern State Hospital, Personal communication.
14. Terman, L. M., and Merrill, A.: Measuring Intelligence, Boston, Houghton Mifflin Company, 1937.
15. Hoskins, R. G.: Biology of Schizophrenia, New York, W. W. Norton, 1946.
16. Bellak, L.: Dementia Praecox, New York, *Grune & Stratton*, 1948.
17. Baganz, C. N., and Norris, J. M.: A Study of Malnutrition in Chronic Schizophrenia, *Am. J. Psychiat.*, 99:534, 1943.

Probability of Relapse In Dementia Praecox

LEWIS DANZIGER, M.D.
Wauwatosa, Wisconsin

A question of importance to the patient and his family after recovery from dementia praecox, is the probability of relapse. Estimates of this probability, when the patient is discharged, are commonly demanded, to the embarrassment of the conscientious physician who has no quantitative data on which to base an opinion. An attempt to furnish such data is made in this paper.

The problem is not different essentially from other problems which can be solved by the construction of a survivorship table, such as is used by insurance companies. It is necessary only to discharge a sufficient number of patients in a certain standard condition, and then follow the rate at which they relapse. Ideally, the state of health of each patient should be determined at appropriate intervals after discharge until he dies or relapses. Such a study would, however, be tedious and expensive and would probably give results only slightly more reliable than the simplified method to be described.

Theory

Suppose that in a certain interval of time, a number of patients be discharged from the hospital recovered. After varying periods, certain numbers of patients will have returned in relapse. If the dates of discharge and return are known for each patient, it is then possible to construct a table showing the percentage of patients still out of the hospital at each interval after discharge. The percentage is the term S_x defined as

$$S_x = \frac{100\ (D - R)}{D} \qquad (1)$$

where D is the number of patients discharged and exposed during the interval x to the risk of relapse, and R is the number of patients returned to the hospital in the interval x. As patients return to the hospital, S_x declines to some minimum value.

With the lapse of time, some discharged patients will die or move away without having returned to the hospital. Others may relapse and enter a private institution. Some may relapse, but remain at home. The S_x calculated from returns will therefore be too large by some undetermined amount. The probability of return, which can be calculated if S_x is known, will be too small, and will represent the minimum rather than the true probability of relapse.

The following theoretical considerations may help to predict an appropriate course for the values of S_x. Let us assume, as suggested in another study (Danziger, 1946) that dementia praecox is caused by an as yet unidentified material, u, which is added to the body at a constant rate, a, and which is disposed of at a rate proportional to the concentration of u. Then the rate of increase of u with time, x, is

$$\frac{du}{dx} = a - bu \qquad (2)$$

where b is the homeostatic constant. This relation has been found to agree with the results of symptomatic and shock therapy in the disorder.

On discharge from the hospital recovered, each patient has in him little or none of the hypothetical u, if the judgment of the clinician has been good. No test now available, however, tells us about the value of a or b on discharge. The terms will have some mean value for the group, probably such that b is larger than a; but for some patients perhaps a is larger than b, in which case eventual relapse is very probable. The time of relapse for each patient will depend on the ratio a/b. The mean values of a and b previously determined for purposes of predicting the response to treatment will not necessarily hold for the purpose of predicting the permanence of recovery. In a group of patients, some of whom are free of u, the mean b will be larger than in a group of patients all of whom have dementia praecox and most of whom are failing to improve under symptomatic treatment.

From Dept. of Psychiatry, Marquette University, and The Milwaukee Sanitarium, Milwaukee, Wisc.

For the individual, this is of no interest. For him the importance questions are

1. Is u increasing.
2. If so, when will it reach a value such that return to the hospital is necessary?

When it reaches this value and he does return, the number of survivors is correspondingly reduced. The number of survivors, then, will depend in some manner on the change in u in each patient, and in the change in the mean u for the group. What is the same thing, the probability of finding the patient still living at home at any given time after discharge will decline in some manner depending on the mean u for the group. In another study, it was found that the probability of recovery declined also as u increased, and that it followed a simple decay law. Assuming a similar law to govern the probability of remaining at home, we have

$$P = P_0 e^{-ku} \qquad (3)$$

where P is the per cent of patients remaining at home;
P_0 is the per cent at home on the day of discharge (in this case 100);
e is the exponential, and
k is a constant. As u increases, then, the probability of finding the patient at home will decline. That is to say, as u increases, the number of survivors will decrease. But u is defined by the solution of (2), namely

$$u = a/b\ (1 - e^{-bx}) \qquad (4)$$

where a and b, it should be emphasized, will have different and possibly fluctuating values for individual patients but stable, mean values for the group. From (3) and (4) it appears that the number of survivors will decline, at first rapidly and then more and more slowly to a level which remains stable and is determined by k and u. As the stable value is approached, the probability of relapse declines until finally the survivors may be considered not more likely than the general population to need hospitalization. When this time is reached, the survivors may be considered to have recovered permanently.

For example, suppose we know that of 100 patients discharged recovered 30 months ago, 40 will eventually return to the hospital and that in fact 38 have returned after 30 months. Of the 62 survivors, then two will eventually relapse. Each survivor then has 2/62 = 0.0322, as his probability of eventual relapse. This is less than the probability of eventual commitment, as calculated by Pollock (1941) for the 1920 general population of New York under age 50. That is to say, the chance of relapse for each survivor becomes very small in comparison with the risk of death in any given interval of time. In the example chosen, it is permissible to make to the family the following prediction: if the patient remains well for 30 months after discharge, his chance of returning to the hospital is not greater than that of a person of the same age and sex of the general population.

The exact time at which the probability of relapse reaches this low value is of no theoretical importance. The question is whether the available experimental data will fit an equation of the type shown in relation (3). To this matter we now turn.

Experimental Results

A. Insulin Shock Therapy

From data published by the Temporary Commission on State Hospital Problems (1944) it is possible to calculate a rough survival table for patients discharged from the Brooklyn (N.Y.) State Hospital after insulin shock therapy. The results are shown in Table 1.

TABLE 1

RETURN TO HOSPITAL AFTER INSULIN SHOCK THERAPY IN DEMENTIA PRAECOX

Time exposed to risk of return in months	No. of patients exposed at beginning of period	No. of patients not returned in period	% exposed patients not returning during period	
			Calculated %	Observed %
12	785	550	70	70
24	627	431	57	68.5
36	473	268	51	56.7
48	266	138	48	51.8
60	120	52	47	43.3
120	.....	.....	45	.....

Between January 1, 1937 and June 30, 1942, 1128 patients were given insulin shock therapy for dementia praecox. Of this group, 897 were sent home, and about 95 per cent

were studied in a social service follow-up between July 1 and December 31, 1942. The condition of the patient on parole, unfortunately, is not shown in the report. The survival data are plotted in Figure 1, and are seen to agree fairly closely with the theoretical equation derived by substituting in (3) the value of u given in (4) and taking logarithms of both sides. The equation then becomes

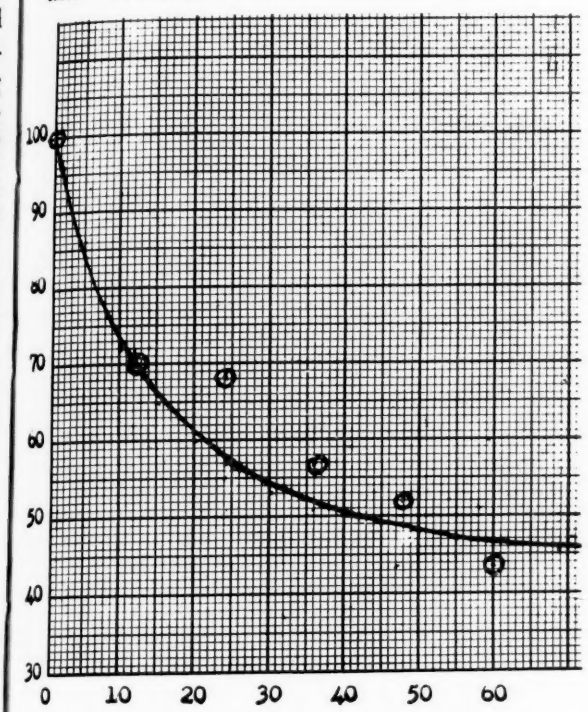


Figure 1. Percent of patients who returned to the Brooklyn State Hospital after having been discharged following a course of insulin shock therapy. Ordinate, the percent remaining at home. Abscissa, time in months between discharge and return. Circles, observed data from Table 1. Curve, theoretical expectation of return where $\log P = 2.0 - 0.35\ (1 - e^{-0.05x})$.

$$\log P = \log 100 - ka/b\ (1 - e^{-bx})$$

Assigning definite values to the constants, this becomes

$$\log P = 2.0 - 0.35\ (1 - e^{-0.05x})$$

where x is the time in months since discharge.

In accordance with expectation, the mean value of b is larger for the paroled group than for the group still in the hospital (Danziger, 1946); for the hospitalized group, the mean value turned out to be 0.027. Later it will be seen that for a group of patients who were considered recovered on the day of discharge from another hospital, b assumes the value 0.07.

The data for the New York patients are in only fair agreement with the theory proposed, although it is seen in Table 1 that the theory predicts in most cases a relapse rate which is of the correct order of magnitude. In view of the careful social service follow-up available to the Temporary Commission, it is probable that the various sources of error previously mentioned do not play an important role. In its report, however, the Commission mentions another factor which may be of importance, namely changes in administrative policy with respect to parole and return. Thus, some of the patients treated in 1937 were considered to have a poor prognosis because they had already been in the hospital for some time. In later years, most of the treated patients had recently been admitted. If the patients had all been in some standard condition at the time of parole, the estimate of prognosis before treatment would be unimportant; but since many apparently were paroled only improved, and some were probably paroled unimproved, the estimated prognosis before treatment might very well affect the relapse rate. The Commission itself suggests, p. 44, that the 1937 group be disregarded when considering relapses.

The very thoroughness of the social service work may also influence the rate of return. The Commission says, p. 34 "it is the practice of the hospital to have the patient return, if only for a brief period of observation, when there is any doubt as to the patient's ability to get along at home." That this would increase the rate of returns is clear but it is not impossible that the application of the policy might vary from year to year.

We are thus in the statistically paradoxical situation of being embarrassed by the very magnitude of the group studied in New York. The larger the group becomes, the more difficult is the application of a uniform administrative policy and the less homogeneous is the group of patients paroled. Yet a smaller hospital system would not be able to afford social service assistance in following and caring for the patients.

The Temporary Commission reported also on the fate of 876 patients in other state hospitals of New York who received symptomatic treatment for their dementia praecox. Of this group, 515 were paroled and about 95 per cent were followed to May 30, 1943. The survival data for this group, recalculated from the Commission's report, appear to say that the chance of remaining at home is greater for the control group than for the insulin group, although the chance of parole is smaller for the control group. The Commission points out (p. 34) that this interpretation is not necessary, however, because

1. The convenient location of the Brooklyn State Hospital, where the insulin group was treated, favors prompt return of the patients.
2. The administrative policy of the Brooklyn State Hospital encouraged prompt return.

It is possible also that the families of the insulin patients felt that the aggressive treatment policy of the Brooklyn State Hospital made prompt return desirable, whereas the families of the control patients were less favorably impressed by the symptomatic treatment given in other institutions.

B. Electric Shock Therapy

Between July, 1942 and August, 1945, 110 patients who had apparently recovered, with or without insight, from dementia praecox after a course of electric shock therapy were discharged from the Milwaukee County Hospital for Mental Diseases. To October 26, 1951, the date of the final check, 53 of the 110 patients had returned to the hospital after periods at home varying from a few days to more than 100 months.

No social service or other follow-up was available for the study of most of these patients after their discharge from the hospital. It is believed, however, that most of those who actually needed further hospitalization returned to the Hospital for Mental Diseases for the following reasons:

It is likely that few patients died at home during the first few years; only patients in reasonably good physical condition were given electric shock treatments, and most of them were under 50 years of age. Of the patients discharged as recovered, nearly all were pleased with the treatment received at the hospital, and in nearly all cases, their families were well satisfied. Few, then, would enter private institutions because they felt they had received poor service at the public hospital.

TABLE 2

RETURN TO HOSPITAL AFTER RECOVERY FROM DEMENTIA PRAECOX UNDER ELECTRIC SHOCK THERAPY

Time exposed to risk of return in months	No. of patients exposed at beginning of period	No. of patients not returned in period	% exposed patients not returning during period	
			Calculated	Observed
			%	%
1	110	103	96	93
3	110	95	89	86
5	110	93	84	85
10	110	87	76	79
12	110	85	72	77
15	110	83	69	75
24	110	80	63	73
36	110	73	59	66
48	110	68	57	62
60	110	66	57	60
74	110	60	56	55
96	24	12	56	50
108	11	7	56	64

Some patients, after recovery, may have moved, but during the period of the study the tendency of migration was not away from Milwaukee County. No restrictions were placed on a patient's movements out of the county or state; but he is considered a resident of the county, regardless of his address, during the period of commitment, which in nearly all cases was for two years after discharge. This long period of parole favors the prompt return of patients needing further treatment even if they should first enter a public hospital of another state. The same parole policy makes it unlikely that relapsed patients will be kept at home for long periods.

The observed and calculated values of S_x for this group are shown in Table 2. Errors may be expected to increase as the time since discharge increases, for various reasons, including: the death of some patients at home; the moving of some patients to other parts of the country; the admission of

some patients to private institutions or veterans hospitals. Another source of error is the slow and often unnoticed change in hospital policy which may subtly influence the type of patient discharged. Finally, as the end of the table is reached, there is the error involved in dealing with small groups; for example, the patients exposed to the risk of relapse for as long as nine years numbered only the 11 who were discharged in 1942; and the patients exposed to the risk of relapse for as long as eight years numbered only the 35 discharged in 1942 and 1943. It turned out that 64 per cent of the 11 patients discharged before 1943 had not returned, while only 54 per cent of the 35 patients discharged before 1944 had not returned at the time of this study. The difference in the percentages, if at all significant for such small groups, may be due to a change in hospital policy in 1943.

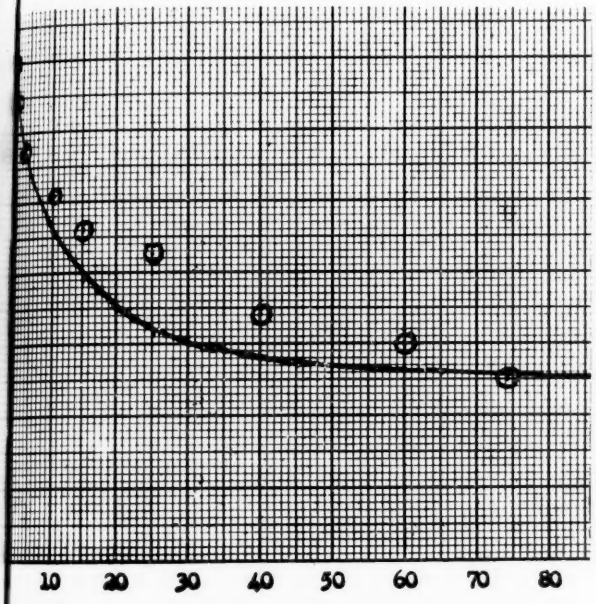


Figure 2. Percent of patients who returned to the Milwaukee County Hospital for Mental Diseases after having been discharged recovered following a course of electric shock therapy. Ordinate, the percent remaining at home. Abscissa, time in months between discharge and return. Circles, observed data, from Table 2. Curve, theoretical expectation of return where $\log P = 2.0 - 0.25\ (1 - e^{-0.07x})$.

The observations are compared in Figure 2 with the theoretical curve

$$\log P = 2.0 - 0.25\ (1 - e^{-0.07x}).$$

The curve is seen to agree closely with the observations for the early months, and to differ from the observations rather more as the time since discharge increases. This type of discrepancy is to be expected from the errors known to be in the data.

It should be noted that the value of b in the equation for the electric shock patients is 1.4 times the value for the New York group, whose condition on discharge was not stated; and is more than 2.5 times the value of b for patients receiving symptomatic therapy in 1933 (Danziger, 1946). These various values of b are in qualitative agreement with the theory here proposed.

From the curve for the electric shock group it appears that of 100 patients paroled as recovered, about 45 will eventually returned to the hospital; and that of the 45, about 42 will have returned within 40 months. Forty months after parole, then, 58 of the original 100 patients will still be at home. Each of the 58 has a probability of eventual return of 3/58 or 0.0517, which is still slightly larger than Pollack's probability (about 0.0515) of eventual commitment for men and women at 20 years of age. Even after 60 months at home, the probability of eventual return to the hospital remains somewhat greater than Pollock's calculated probability (about 0.034) of eventual first admission for the general population at 50 years of age. It is, then very difficult to say that a patient given electric shock therapy has recovered permanently in the sense that his chance of requiring hospitalization is no greater than that of any other member of the general population of the same age and sex. However, after remaining at home for five years, the patient who was well on discharge is only a little (about 3 per cent) more likely to require eventual hospitalization than any person 50 years of age.

Similar calculations for the insulin group, gives roughly similar results for patients who remain at home for five years.

Conclusions

The families of paroled patients are nearly always concerned about the possibilities of relapse and return to the hospital. For patients who have been given shock therapy for dementia praecox, the following answers to the questions about prognosis appear to be reasonable:

1. If the patient has recovered under electric shock therapy, he has, on the day of parole, about 45 chances in 100 of returning to the hospital eventually; but
2. If he remains at home for about five years, his chance of coming to the hospital is roughly of the same order of magnitude as that of any person of the same age and sex in the general population.
3. If the patient has had insulin shock therapy, on the day of parole he has (disregarding his condition on parole) about 55 chances in 100 of returning to the hospital eventually; but
4. If he remains at home for about five years, his chance of coming to the hospital is roughly of the same order of magnitude as that of any person of the same age and sex in the general population.

These conclusions are derived from a theoretical equation which is in fair agreement with the available experimental results.

In individual cases, the attitude of the family and community may influence the probability of return in a manner not taken into account by the theoretical equation. The equation, it should be emphasized, holds only for groups of patients. Its importance is in the fact that it is derived from the same theory which led to a prediction of the results of symptomatic and shock therapy in dementia praecox, and which suggested a reason for the high death rates in psychotic patients.

Author's Note: The expenses of this investigation were defrayed in part by the Ada P. Kradwell Memorial Foundation.

This paper is to be published also in the Journal of Insurance Medicine.

REFERENCES

Danziger, L.: Some Theoretical Considerations of Dementia Praecox. *Dis. Nerv. Syst.* 7, 357, 1946.

Pollock, H.: Mental Disease and Social Welfare. *State Hospitals Press*, Utica, N. Y., 1941.

Temporary Commission on State Hospital Problems, 1944. Insulin Shock Therapy. 105 East 22nd Street, New York 10, N. Y.

Pregnancy In Lobotomized Schizophrenia

W. G. ELIASBERG, M.D.

New York, New York

The law and the decisions of the courts in cases of artificial abortion have changed very little in the last 100 years. T. E. Harris has given a survey of those indications that seem to be recognized by the courts and the medical profession as requiring a termination of pregnancy.

In all states it is the principle accepted by the legal profession and physicians that abortion is legally permissible, if it is necessary to preserve the life of the mother or to prevent serious physical injury such as impairment of sight or hearing. Four states (Colorado, District of Columbia, Maryland, and New Mexico) make provision for the future health of the mother, not only for her life or serious physical impairment.

A problem which has had some attention is that of the woman who had one or more children with Sachs Tay amaurosis should continue a subsequent pregnancy. Similarly the question may be raised whether a woman over forty, with a previous mongoloid child, who has a 6 per cent statistical risk of having another mongoloid child, should be allowed to have an artificial abortion.

Psychiatric cases, with psychoses such as manic depressive psychosis or schizophrenia are another important group requiring a decision as to continuance of their pregnancy. Gregory Zilboorg writing in 1928, states his views as to manic depressives: "In women who are disposed childbirth appears to be the nodal point of the conflict and the causative agent of the psychosis."[2,3]

While normal childbirth is not an unusual risk to health in a normal woman, the functions which in their totality make up childbirth seem to constitute an added risk to the mental health of the woman who is either suspected of schizophrenia or is or was manifestly schizophrenic.

In 1930 I published a report based on a questionnaire[4] concerning pregnancy in ma-

nic depressive psychosis. Such cyclothymic disorders are not at present sufficiently appraised in clinical medicine, although for years a host of vague, persistent and returning disorders, for which the patients will see general practitioners, internists, and gynecologists have been known to disappear abruptly, with or without therapy, only to return for apparently no reason. The connection between cyclothymic disorders and abortion may be as follows:

1) Spontaneous abortion caused:

   a) by depressive changes of the general vital tonus; this phase is known to cause disorders such as amenorrhea, sterility, cessation of lactation;
   b) The manic phase with its violent changes of the general tonus and especially the tonus of the motorium could likewise cause spontaneous abortion.
   c) Furthermore in both the depressive and the manic phase there may be an increased proneness to accidents leading to abortion.

2) Artificial abortion may psychologically be caused by:

   a) the depressive phase

      It is characteristic in the depressive phase that all difficulties or even mere expectation of difficulties are enormously exaggerated and aggravate the patient. Thus, too, the functions of pregnancy, childbirth, nursing, and rearing the child may appear unbearable to the depressed patient.

   b) the manic phase

      It is known that inhibitions against criminal actions are diminished in the manic phase. In this way a woman who would not think of a criminal act in the depressive or the normal phase might lightly overcome inhibitions against criminal abortion.

The relationship between psychotic conditions and artificial or spontaneous abortion certainly requires more investigation. What methods should be used in this inquiry? Wherever matters of the mind, matters psychological, are involved we are not able to submit the actual material to extensive measurements. Therefore, another method, that of statistical reference, has gained overwhelming importance in medicine in general and in psychiatry in particular. The acid test, however, of any theory is practice, the individual case. This holds even more true in diagnosis than in treatment. In treatment of the patient the physician may in many cases concentrate on the biological aspects of the disease. If, however, the question is raised as to the social, legal and economic reflections of the illness, which is always a part of the expert's considerations, then the human being cannot be considered the mere intersection of biological lines. The actual case and particularly the case in which an opinion is to be rendered is the crucial test in the verification of a theory. The reasoning is forced to envisage the real problem; it is put to trial in the single case with all its unexpected, manifold, concrete aspects. We therefore feel that the publication of the following case, in which the reasons for recommendation of abortion are set forth in detail, is justified. Moreover, practitioners, gynecologists, psychiatrists, lawyers and the courts should pay heed to the fact that legal, justifiable and ethical indications for artificial interruption of pregnancy are frequently of psychiatric nature.

Mrs. X, a divorced woman, 40 years old, poses the question whether she should be allowed to continue her pregnancy, which is in the second month. My opinion was sought because Mrs. X had been previously hospitalized in 1937 for dementia praecox, hebephrenic type and remained in hospitals until April 29th, 1949, a period of 12 years and had a bilateral prefrontal lobotomy in 1949 with uneventful surgical course.

Family History: Father came from Hungary, was always excitable and nervous; in father's family there had been several suicides; 10 years before father's cousin had leaped from a bridge to his death. Mother is of German descent; knows of no abnormalities in her family. There is one older half-sister, 45, mother's daughter, married, healthy and apparently well adjusted.

Personal History: Patient was beautiful as a young girl and quite spoiled. She wanted to associate with better class people. Graduating from high school she took a business course and then worked as a secretary. She was married in 1934. There were difficulties from the very beginning and the patient thinks she fell ill becaue of them. She became very violent and had to move back with her parents, but could not stay there. She was hospitalized in 1937 with diagnosis of dementia praecox, hebephrenic type; she received repeated series of electric and insulin shock without lasting benefit. She recalls her stay at Binghamton State Hospital but denies recollection of Rockland State Hospital where she was confined from 1937 to 1942; nor does she know that she attacked members of her family. After the lobotomy in 1949 she became quiet, nei-

ther talkative nor restless. She had never had epileptic fits; food intake was good, her weight increasing to 150 lbs. There were no alcoholic excesses. In November 1949 she returned to her parents, enrolled in a refresher course in secretarial work and tried to work. Since that time she had many jobs, none of which was she able to keep for long. She was late repeatedly; could not get up in the morning and had frequent quarrels. Employers found her of friendly disposition but not able to do her work.

Present Complaints: The patient herself has no complaints. She insists that she is all right. She reports with a friendly smile that she has no headaches, her appetite is good, bowels regular, she has put on some weight, would like to be careful about her food; in fact she says because she watches herself she has lost several pounds. She has no troubles of pregnancy such as nausea, etc.

Physical Findings: Height: 62 in.; weight: 129 lbs. She is good looking; her skin is smooth and soft as a girl's. Her chestnut brown hair has a few white strands about 3 fingers anteriorly and 2 fingers above the upper ear pole on the right and the left temple, pits of bean size in the bone from the operation in 1949; skin in this region is not irritated, the pits are covered by hair. Teeth are in good condition, gums not irritated; tonsils and pharynx slightly irritated; thyroid not increased. Her skin is dry, no rashes; dermographism: first red, then white, not increased. Pulse 80 in sitting position, equal; blood pressure: 116-68; heart in normal borders, without murmurs or thrills; lungs: auscultation normal, border normal. Ophthalmoscope examinations: Both eyes deep physiological excavations, vessels not interrupted, slight astigmatic form of the disks; pupils respond directly and indirectly to light; movement free; no nystagmi. Reflexes: arm reflexes not increased, equal on both sides; patella reflexes normal. Encephalogram normal.

Mental Findings: It is characteristic that the patient does not mention any complaints.

About the incident which led to the pregnancy she related that two months previous she went to a dance with a girl friend and was introduced to a stranger, who bought her several drinks. She does not remember anything that happened thereafter. When menstruation ceased she was taken to Dr. W. and found pregnant. When asked whether she wanted to have the child she said: "Oh no, I cannot have the child, I must think of my family and the disgrace!" There is absolutely no congruent affect, she grinned and that is all. When it is suggested that she have the child she quickly falls in with the idea. The man who fathered the child has in the meantime repeatedly called her, has asked her to marry him and wants her to carry the child. He has a civil service position and is in a position to take care of a family. Asked whether she would like to marry him she says: "I don't know, I first have to find out whether I love him."

When it is explained that if the pregnancy is interrupted, sterilization also should be performed she cannot be made to understand. Her mother says in her presence: "She need not know; one must not tell her such things." The patient smiles and says: "Oh, mother is always that way, she does not let me know anything."

Her behavior is not that of a grown-up person, who has a serious interest to learn what is to happen to her body. Much less is there any indication of a conflict such as would be experienced by a normal woman who is faced with the prospect of not only losing her child but her fertility as well.

The relationship between herself and her mother (age 74) is just the opposite of what one would expect. It is not the grown-up daughter taking care of her aged mother, but a mother caring for her youngster. This picture is rounded out by her friendly incompetence and laziness on her job. Contrariwise, she will say that she has to earn money to help her parents; in fact, mother has to drive her out of bed every morning and her work is practically worthless.

It should be noted that her appearance is neat, that she dresses according to what one would expect in a secretary; she takes care of her outward appearance. It is known from other conditions such as aphasia that the outward forms of social contact, of politeness, are astonishingly well preserved at a time when efficiency on the job is diminished.[5] Likewise lobotomized patients may keep up the shell of social contact when the core has gone. On the whole the character type of our post-lobotomized patient is in keeping with the pictures given by practically all observers.[6,7,8,9]

While there are rare cases where the patient becomes fully responsible—even in such cases very often alcoholism is observed—the following is a resumé of typical character traits and attitudes: lack of self-consciousness, child-like pleasure in simple things, facetiousness, sarcastic remarks, emotional immaturity, inability to assume adult responsibilities.

The result of the tests, administered to this patient might not at first seem to fit in with this outline. The patient showed unusually good immediate retention of spoken figures up to 9 digits. She also showed good memory in the association test; she was able to reproduce her own reaction words after half an hour and more. In the association test she also showed linguistic volubility, although a tendency to repeat reactions was noted. Her spelling was excellent. The characteristic factor in the association test was the complete absence of any signs of emotional complexes, such as might

have been expected with pregnancy or mental disease.

Thematic Apperception Test:

Patient shows very flat reactions. She describes objectively; there are few remarks that point to any emotional understanding of the situation. Characteristic is the reaction to picture 3 G.F., where a young girl is shown standing in utter dejection and covering her face.

"Someone in great sorrow. She is crying." (Why?) "Someone close to her has passed away." Then she turns the picture and looks at the back. (What else could it be?) "She has heard some bad news." (What?) "She has to leave her country. She has to go to jail for something, for committing a crime. Maybe she robbed someone." (That is wrong. What else could it be?) "Maybe she is pregnant."

At this point her mother asks: "What about yourself?"

Patient smiling: "Mother is just wisecracking."

After much prodding she becomes aware of her pregnancy but it does not register with her emotionally.

The same is true for picture 2, where a pregnant woman is seen. She first does not notice her at all. She says:

"This is a picture of a young girl who lives on a farm; she is disturbed at what she sees. She looks rather disgruntled at the world." (What does she see?) "She sees the man working. The other woman is idling, not doing anything." (Why?) "Maybe the woman is tired." (Don't you see anything else?) "The tummy is bulging, maybe she is pregnant."

Rorschach Test:

Patient has few reactions on the Rorschach test. no original responses, no colorshock. The very typical card No. 5, that is rarely missed, is not answered.

"I don't know what this would be?" (Finally) "A bat?"

To No. 8 her answer comes after a long interval: "It does not make sense to me, I see different colors, Grey, Blue, Rose, Orange, but it does not mean anything."

After the experiment is finished, she says: "It looked like squirrels or mice. I did not want to say it, because I'm afraid of mice and I don't know much about squirrels."

In the usual inventory and so-called intelligence test the patient scored high. But E. A. Strecker found that psychological testing does not reveal measurable intelligence defects in lobotomized patients. It has, however, been feasible to elicit and demonstrate typical intelligence defects in a special test devised to test creative thinking.[10]

From beginning to end (16th exp.) the patient is alert to what is going on and sticks to the data that can be perceived. She also notices esthetic qualities and is voluble in verbalizing her perception, but she remains glued, as it were, to the perception and does not achieve the abstraction of the rule which normal 3½ to 4 year old children do achieve, that of two colors one bears a certain mark and the other does not.

The very nature of her defect appears in the projective tests, because the patient has no adequate emotions. She is unimaginative to an astonishing degree; it requires much prodding to get her to project herself and even then her answers appear poor and silly.

Diagnosis: Typical post-operative mental status after lobotomy. At present no active schizophrenia.

Recommendation as to Pregnancy: The question of interruption of pregnancy has to be considered on the basis of the prognosis a) for the mother, b) for motherhood, c) for the child. It is in the prognostic deliberations as to the patient herself that statistics have a proper place. Having elicited as much of the circumstances of the individual case as possible we have to assess their statistical weight. We must ascertain the prognosis of schizophrenics treated a) by the older methods and b) by lobotomy. The literature, however, is scanty and unsatisfactory. The most modern books such as L. Bellak, "Dementia Praecox" (Grune & Stratton, N. Y., 1948) and M. Greenblatt, "Studies in Lobotomy"[8] do not give the answer to the questions of frequency of relapses in treated cases and frequency of relapses in relation to pregnancy. E. A. Strecker[9] wrote: "One patient, apparently free from symptoms, has married and had a baby, though, of course, against our advice." Strecker undoubtedly was impressed by the risk which pregnancy imposes on a lobotomized patient.

Investigators for the British Board of Control on the basis of 1000 cases published the results of their studies as to relapse frequency of lobotomized patients.[11] Of the 1000 cases, 599 were schizophrenias, among which 11.5 per cent of discharged patients relapsed; of those remaining in the hospital 3.7 per cent relapsed making a total of 15.2 percent relapses without the complication of pregnancy.

Statistically, then, the risk to Miss X of relapse is at least 15 per cent and it can be said with reasonable probability, much higher because the functions of childbirth represent an added risk. From this point of view it is understandable that an experienced psychiatrist like Strecker would have dissuaded marriage and pregnancy.

What is the prognosis as to successful motherhood? Our patient, as so many other lobotomized patients, cannot be trusted with the responsibility of the adult. She is in fact on the emotional level of a child. She herself has to be babied. How could she be a mother?

Prognosis for the child: There are certain hereditary diseases such as Tay Sachs amaurosis where the fact that a mother has born one or two so stricken children will warrant interruption of pregnancy and permanent sterilization. While schizophrenic heredity does not in itself require such a severe measure, the fate of the child would be doubtful due to hereditary and patho-physiological factors, among which the age of the mother is of importance. According to recent findings[12] a woman who becomes pregnant after 40 runs the statistical risk of approximately 6 per cent of having a mongoloid child.

On operation the fetus was found to be older than expected (4½ months). Sterilization was therefore not performed. The patient was observed by the gynecologist for 5 days and he noticed the difference in her emotional response to the operation from that of other women. She was exceptionally quiet, there were no signs of any conflict, she did not even talk about what had been done. She seemed totally indifferent.

Summary

Indications for artificial interruption of pregnancy are often of a psychiatric nature.

A case of a patient, suffering 12 years from schizophrenia, was lobotomized and became pregnant in the first year thereafter is presented. The reasons why the pregnancy should be interrupted have been discussed. They are: danger for the mother, demonstrable inability of the mother to live up to the responsibilities of motherhood and dangers of hereditary tainting and neglect for the child. Psychological or social psychological conflicts have not played any part in this case.

REFERENCES

1. Harris, T. E.: The Functional Study of Existing Abortion Laws; *Col. Law Review*, Vol. 35, Jan. 1935, No. 1, pp. 85-97.
2. Zilboorg, G.: Malignant Psychoses Related to Childbirth; *Am. J. of Obstetrics and Gynecology;* Vol. XV, No. 2, p. 145, Feb. 1928.
3. ————: Post Partum Schizophrenia; *J. of Nerv. and Ment. Dis.;* Vol. 68, No. 4, Oct. 1928.
4. Eliasberg, W.: Fragebogen betreffend Zusammenhang des Aborts mit zyklothymen Stoerungen (Questionnaire concerning connection of abortion with cyclothymic disorders); *Arch. f. Frauenkunde*, Bd 16, H. 3, 1930.
5. ————: The Social Implications of Dysphasia; *J. of Nerv. and Ment. Dis.*, Vol. 105, No. 5, 1947.
6. Bennett, A. E.: Prefrontal Lobotomy in Chronic Schizophrenia; *J.A.M.A.*, Vol. 123, No. 13, Nov. 27, 1943, p. 809 ff.
7. Freeman, W., and Watts, J.: Psychosurgery; *Ch. Thomas Publ'r*, 1942.
8. Greenblatt, M., and Co-workers: Studies in Lobotomy; *Grune & Stratton, Inc.*, New York, 1950.
9. Strecker, E. A., and Co-workers: A Study in Frontal Lobotomy; *Am. J. of Psychiat.;* Vol. 98, No. 4, Jan. 1942, pp. 523, ff.
10. Eliasberg, W.: Psychology and Pathology of Abstraction; *Johann. Amb. Barth Verlag*, Leipzig, 1925.
11. British Board of Control: Report on Prefrontal Lobotomy in 1000 Cases; *His Majesty's Stationer's Office*, London.
12. Böök, J. A., and Reed, S. C.: Empiric Risk Figures in Mongolism; *J.A.M.A.*, Vol. 143, No. 8, June 24th, 1950.

Neurological Clinical Pathological Conference

of the

Cincinnati General Hospital

CHARLES D. ARING, M.D., *Editor*

CASE NO. 257225

Presentation

An 11-year-old colored girl had suffered occasional headaches since early childhood but her past health and development were otherwise normal except for uncomplicated whooping cough and measles. In September 1949 headache became more frequent and severe and then could be localized by the patient to the bifrontal region. The headaches were occurring every few days. They were present on awakening and decreased in severity as the day progressed. In October episodes of repeated vomiting began to accompany the headaches. For the first time she noted photophobia and had short periods of double vision. Later in the month she was sent home from school for an eye examination because of visual difficulty.

On October 28 visual acuity on the right was 20/50, left 20/30 —1. The cups in the optic discs were shallow and the fundi were hyperemic. On December 7 visual acuity on the right was 20/100, left 20/25 —1 and there was 2 to 3 diopters of papilledema bilaterally. Perimetry showed slight concentric constriction of the visual fields and enlargement of the blind spot in each field. There was some stiffness of the neck. Roentgenograms of the skull revealed the pineal gland to be calcified and slightly displaced postero-inferiorly and to the left. An electroencephalogram showed moderate diffuse slow activity of slightly lower amplitude than the basic 10 per second occipital (alpha) rhythm, the greatest amount of slowing being in the right occipital region. Several blood Kahn tests were negative.

On December 14 there was dilatation of both lateral ventricles and of the anterior portion of the third ventricle on ventriculography. (The posterior portion of the third ventricle, the aqueduct and the fourth ventricle did not fill with air.) There followed a left subtemporal decompression and a third ventriculostomy on the same day. The patient remained lethargic. Following this there was tachycardia and fever which fluctuated from 99.2 to 105 degrees F. Intramuscular penicillin was begun on December 14 and was continued during most of the remaining illness. On December 20 there was a notable depression of the level of consciousness. Severe nuchal rigidity developed and the pupils became constricted. Bilateral ventricular tap released clear fluid under high pressure followed by immediate improvement in the general condition. This cycle of events was repeated during the night of December 20 and on the morning of December 21 a bilateral Torkildsen procedure was carried out.

Fever and nuchal rigidity persisted and on December 28 paralysis of upward gaze was observed. A lumbar puncture on this date revealed an initial pressure of 350 mm., the fluid contained 1340 leukocytes per cmm., predominantly lymphocytes. No organisms were seen in the stained sediment of the fluid and none grew on culture.

On December 29 one cc. of phenolsulfophthalein solution was injected into the left lateral ventricle. When the dye failed to appear in the right lateral ventricle one cc. was introduced into the latter chamber. The dye appeared in the lumbar subarachnoid space 20 minutes after it had been instilled in the left lateral ventricle. On December 30 deep roentgen therapy to the region of the third ventricle was instituted and this was continued through January 24, 1950, for a total of 3200 roentgen units.

A wound infection of the occipital incision was noted on December 31. A persistent defect formed at the site of the incision which continued to discharge white purulent material. On January 10, 1950 both pus and cerebrospinal fluid were issuing from this defect. Lumbar punctures were performed at frequent intervals following the tap of December 28. The cerebrospinal fluid pressure varied from 110 to 290 mm. Twenty to 25 cc. of fluid were usually removed at each tap and 15,000 units of penicillin instilled intrathecally. On January 3 the cerebrospinal fluid leukocyte count fell to 670 per cmm., 36 per cmm. on January 12 and 2 per cmm. on January 17. Lymphocytes formed the predominant cell type in each examination. A specimen of lumbar fluid collected on January 11 contained 1650 mg. per cent of protein.

The patient was responsive until January 5 when her level of consciousness began to decline progressively. From January 12 to 19 she would sometimes respond to her name and at other times would respond only to painful stimuli. On January 19 respirations became rapid and labored and she was totally unresponsive. A cerebrospinal fluid pressure of 580 mm. was recorded on January 21. On January 24 gram negative bacilli were found in the sediment of the cerebrospinal fluid and bacteria of the aerogenes group were grown on culture. The patient expired on January 25, 1950, the forty-ninth hospital day.

Differential Diagnosis

Dr. Harry M. Salzer: This 11-year-old colored girl with complaint of headache may be considered from several points of view, and I will discuss localizing clinical findings,

roentgen studies, and evaluation of the cerebrospinal fluid studies before considering etiology.

The first localizing symptoms were referable to the oculomotor and visual systems. These included double vision, photophobia in October, and later failing vision with papilledema and paralysis of upward gaze. The photophobia might represent local disturbance in the eye, or as seems to be the case here, it might occur as the result of some alteration in pupillary control. The periods of diplopia suggest oculomotor nerve palsy though there is no indication as to which nerve is involved. Later, on December 28, paralysis of upward gaze was noted. This is known as Parinaud's syndrome and occurs with lesions of the superior colliculi and also in subthalamic lesions. The relatively good visual acuity in the left eye in the presence of swelling of the nerve head means that this was not optic neuritis or other local disturbance in the optic nerve as may be seen in multiple sclerosis. The papilledema with confirmatory evidence of the enlarged blind spot then raises the possibility of an expanding lesion producing increasing intracranial pressure. The headache and vomiting doubtless relate to this. The stiffness of the neck which was described on December 7 need not indicate a generalized inflammatory process since this may occur also with lesions of the midbrain and posterior fossa.

Thus on the basis of examination and history we may consider that a lesion is present within or pressing upon the midbrain. These findings alone do not give us a definitive clue as to the nature of the lesion. Though the progressive course would suggest an expanding lesion which had blocked the free flow of cerebrospinal fluid, other studies are needed to establish a diagnosis. Report of the roentgen study is in order at this point.

Dr. C. J. Miller: I would first like to discuss the initial plain films of the skull which demonstrate the pineal gland calcification. By standard measurements we see that it is displaced between 4 to 5 millimeters to the left side, and it is also displaced backward and downward. In an 11-year-old child this calcification is an abnormal shadow. In persons over 20 years, 60 per cent show calcification of pineal gland, but in children under 10 and 12 years of age any calcification in the pineal gland should be considered questionably normal and a pinealoma should be suspected. Now, as to whether this represents calcification in the pineal gland or calcification in a tumor, we do not know. The downward and backward displacement are of no help in differentiating whether calcification is in a tumor, which is found in from 20 to 50 per cent of cases, or whether it is in the pineal gland. There is no radiographic evidence of increased intracranial pressure on the plain films. However, on the ventriculogram it is apparent that there is rather marked dilatation of the lateral ventricles and also dilatation of the third ventricle, the reason for this being apparent when we come to the lateral films. The septum pellucidum and third ventricle show no deviation from the midline. Lateral films confirm the dilatation of the lateral ventricles and third ventricle and show no evidence of filling of the aqueduct or fourth ventricle. The reason for this is a mass in the posterior portion of the third ventricle, measuring 2.5 x 3.0 cm.; the calcification is seen eccentrically located (posteriorly) in this mass.

Radiographically, a pineoloma is the most likely diagnosis; other lesions to be considered are a teratoid tumor or an ependymoma.

Dr. Salzer: In light of the radiographic findings one can say that this is a lesion which is outside of the substance of the brainstem, probably in the midline. Undoubtedly, because of the presence of midbrain signs and papilledema, no studies were done on the cerebrospinal fluid prior to ventriculography. When it was performed on December 28, the suspicion of increased pressure was corroborated. The leucocytes which were found in the fluid were believed to follow on the operative procedure. Possibly an inflammatory lesion in the posterior portion of the third ventricle may have been the primary cause of the cells.

The lumbar puncture pressure, measured frequently following the tap on December 28, was variable, ranging between 110 mm. and 290 mm. These pressure measurements deserve some word. If the taps had been done frequently, the pressure might be ex-

pected to have been low. The pressure might also hinge on how the Torkildsen by-pass was functioning; variance in the cerebrospinal fluid pressure might result from its varying function. The protein increase was due to cerebrospinal fluid block. Perhaps the longitudinal sinus drained off cerebrospinal fluid before it had a chance to get down to the lumbar sac, and the factor of dilution was therefore reduced. Possibly the high protein resulted from the destructive effects of roentgen therapy given earlier, but that would not have been associated with such a large increase. The gram negative bacilli which were found and also the aerogenes group were probably introduced by the surgical procedure. Death seems to have been from the effects of increased intracranial pressure and secondarily from bronchial pneumonia.

Now, with all the data available, the lesion—whatever it is—is localized to the region of the posterior portion of the third ventricle and upper midbrain area, and the lesion which most commonly occurs in this area is pinealoma. There are other types of tumor which occur here; for example, cholesteatoma and teratoma. Another possibility is that this patient had a tumor growing from the right subthalamic area, possibly a glioblastoma with extension into the upper midbrain. Still rarer would be benign colloid cyst of the third ventricle. A meningioma in this area would be uncommon. Medulloblastoma would be unlikely to extend to the midbrain. Other types of tumors are unlikely. The possibility of an inflammatory lesion in this area must be considered. Such disorders as tuberculoma are possible as are echinococcic cysts or other rare types of parasitic inflammation.

Tumors in this area produce two types of symptoms. One group of symptoms arise from the local effect of the tumor on the midbrain; the other symptoms are those of the general effects of increased intracranial pressure. The local effects are, as might be expected, due to involvement of the nuclei located here, and we may see ptosis, ophthalmoplegia, Parinaud's syndrome, or there may be altered pupillary reaction. Ataxia and tremor may be present because of involvement of cerebellar pathways. There may be impaired hearing as just below are pathways transmitting hearing.

As part of the general effect there may be occipital headache, pain and stiffness of the neck, and retraction of the head. In young males particularly there is a condition of precocious physical development. In no adult case has there been any such genital alteration. Harris and Cairns[1] have observed a likeness between pinealoma cells and the spheroidal cells of testicular origin.

The roentgen therapy was therapeutic heroism. Something had to be done.

A summary of diagnosis and treatment of pineal tumors was published by Horrax.[2] He described 22 cases, 14 of which were confirmed by operation or autopsy. He noted headache as the chief complaint, visual impairment as a late symptom. Occasionally there were signs of cerebellar involvement and sometimes there was diabetes insipidus. In 2 of 5 cases of diabetes insipidus studied by Horrax, pineal tumor was verified histologically. Papilledema was usually considerable, but, of course, had no localizing significance. There was loss of conjugate upward movement of the eyes, as described in this case, and loss of pupillary reaction to light occurred with nearly normal visual acuity.

Horrax felt that roentgen therapy was the treatment of choice. Many of these patients had to have subtemporal decompression first, however. If roentgen therapy was not beneficial, he advised operation with attempts to remove the tumor. He had operated 10 of the 22 patients described in this article; three were alive ten, five, and three years post-operatively. Although these are good results considering the locale of this tumor, the editor of the 1949 Yearbook of Neurology, Psychiatry, and Neurosurgery, Doctor Percival Bailey, agreed with Harvey Cushing who wrote that he had never exposed a pineal tumor well enough to remove it. So, we conclude that this patient had a pineal tumor, and there was no chance to remove it.

Discussion of Pathology

Dr. Murton Shaver: The autopsy was performed 4 hours after death. The brain weighed 1240 grams. The dural cap over the postero-mesial portion of both hemi-

spheres presented a small incisional opening 3 cm. from the midline in the posterior parietal regions bilaterally with small rubber catheters emerging through these openings. The right catheter was anchored to the dura with fine silk sutures.

The cerebral hemispheres appeared symmetrical, showed generalized flattening of the convolutions with normal pattern. The leptomeninges generally appeared thin and contained congested veins. Emerging from the cerebral hemispheres in the posterior parietal region bilaterally at sites corresponding to those described in the dura were the two small catheters, the tissue around the one in the right hemisphere showed some softening for a radius of 5 to 6 mm. There was no subarachnoid effusion. The median cleft showed adherence of the two frontal lobes across the midline, and at this site the tissue was soft and poorly fixed.

There was brownish staining of the leptomeninges overlying the optic chiasm and the chiasm appeared markedly thickened, white, and soft to palpation. There was an accumulation of yellowish gray material in the leptomeninges over the cerebral peduncles and the pons extending backward over the medulla and cerebellar peduncles. There appeared to be some notching of the hippocampus on the right, but there was no definite shifting of the pons or medulla which appeared to lie in the midline. There was no evidence of a cerebellar pressure cone.

The vessels at the base were obscured by the thickened leptomeninges.

The catheters were removed and the one on the right was found to extend to a depth of 4.5 cm. although a suture was anchored to the dura at 6.5 cm. from the tip. The catheter on the left extended to a distance of 11 cm. from the suture anchoring it to the dura.

The cerebrum was separated from the brain stem in the upper third of the pons, and it was sectioned coronally at 1 cm. intervals. These sections were poorly fixed, and the white matter generally appeared edematous. There was no shifting of the midline structures. A large fifth ventricle was present. The lateral ventricle appeared large, measured 3 x 1.5 cm. and was lined by walls in which the ependyma was largely obscured by plaques of soft grayish yellow gelatinous material and in a few cases by flecks of adherent blood clot. The left temporal horn contained a firm blood clot in the form of a cast. The third ventricle was enlarged and lined by similar gelatinous material as that found in the lateral ventricles while the left occipital horn contained blood clot and the surrounding tissue was markedly softened and showed petechial hemorrhages scattered throughout the margin of a large cystic cavity with no evidence of ependymal lining. This had the gross appearance of an abscess measuring 2.5 cm. in diameter. Communicating with the floor of this cavity was the puncture wound from a ventricular needle through which the catheter had passed. On the right side lying just below the catheter sinus was a small cavity lined by a somewhat fibrous yellowish gray membrane. This cavity was somewhat collapsed and measured 1.8 x .8 cm.

A section passing through the upper portion of the aqueduct of Sylvius showed it to be lined by gelatinous material similar to that found in the third ventricle and a large quantity of similar tissue was found filling the posterior extent of the third ventricle in the region of the pineal gland. It was possible that a small quantity of similar material extended out along the veins of Galen posteriorly. It appeared that the upper extent of the aqueduct of Sylvius was blocked by this yellowish gray gelatinous tissue although this could not be definitely proven. No adhesions extended across the aqueduct which was generally slightly widened.

Sections through the brain stem and cerebellum at 1 cm. intervals revealed only moderate enlargement of the fourth ventricle which measured 2 x 2.5 cm. in its broadest extent and was covered by gelatinous material similar to that found in the other ventricles.

Numerous blocks of tissue were removed from frontal, temporal, and occipital cerebral cortex, together with sections from the region of the basal ganglia and midbrain. In all these sections the cortical surfaces were covered by leptomeninges in which the vessels were congested. They showed only a

slight infiltration with a few endothelial cells and occasional lymphocytes. The cortex showed degenerative changes in the nerve cells with swelling and chromatolysis in some of the cells, while others showed ischemic or sclerotic changes. Neuronophagia and satellitosis occurred in a few cases in the deep layers. The vessels throughout the gray matter were congested, but otherwise not remarkable.

Sections bordering on the lateral and third ventricles showed marked granulomatous infiltration of the subependymal tissues. The vessels were congested and occasionally small perivascular hemorrhages were seen. The vessel walls in many cases were necrosed or hyalinized while in large numbers they showed proliferation of endothelial cells and appeared to be incorporated in the inflammatory exudate surrounding them in the perivascular spaces. The cells in these areas consisted largely of lymphocytes, endothelial cells and numbers of plasma cells. In a few instances this inflammatory infiltration extended into the surrounding parenchyma for a short distance. The ependymal cells in many areas showed evidence of proliferation with swelling. In other areas, the cells were lost and the surface was covered with an exudate similar to that described around the blood vessels. Here large numbers of histiocytes or endothelial cells containing occasional red blood cells and other granular and amorphous material were seen. Some of these cells were also found in the subependymal areas where the ependyma had been eroded. The exudate was infiltrated by large numbers of fibroblasts in some areas, while in others the tissue seemed to be composed largely of lymphocytes, plasma cells and endothelial cells without definite tubercle formation or caseation. Sections through the posterior portion of the third ventricle showed the lumen of the ventricle completely occluded by this exudate, while the walls of the ventricle showed extension of similar exudate around the vessels for some distance deep to the ependyma.

Sections through the occipital cortex in the region of the catheters showed a rather similar type of inflammatory change with, however, areas of necrosis and large numbers of histiocytes scattered throughout this tissue. There was no definite abscess wall, although some of the blood vessels in this region showed proliferation and budding and the tissue deep to this showed a rather cellular appearance with increased numbers of glial cells.

All of these sections were stained with Ziehl-Neelsen, phosphotungstic acid, eosin methylene blue, and other bacterial stains. None of these methods demonstrated any organisms on repeated examination by numerous observers.

Sections made through the posterior extent of the third ventricle and upper pons demonstrated what was thought to be the pineal gland with granulomatous tissue surrounding the gland and infiltrating it. In some places this structure was hard to define. Calcium deposits were present in this tissue and the inflammatory exudate was found to surround the blood vessels in this region.

Sections made through the midpons and upper medulla demonstrated marked inflammatory changes in the blood vessels in the subependymal region with proliferation of endothelial cells and numbers of lymphocytes and plasma cells lying in the perivascular spaces. Here again the blood vessel walls appeared to be incorporated in the inflammatory changes surrounding them, and in some cases this inflammatory change extended deeply into the subjacent tissues. The ependymal surfaces were better preserved in the fourth ventricle, although eroded in some areas, and there was a thin film of exudate similar to that seen in the third ventricle overlying the ependyma. Numerous hemorrhages were seen in scattered foci around the vessels lying deep to the floor of the fourth ventricle and in some cases lying in the roof of the fourth ventricle. The meninges at the base showed a marked inflammatory change similar to that found in the ventricles with granulomatous appearance. This was most marked in the meninges at the base of the medulla, but was also present to a lesser extent overlying the pons. This inflammation at times appeared to extend along the vessels into the substance of the brain stem. The leptomeninges over the cerebellar foliae showed little

inflammatory infiltration, consisting in small clusters of endothelial cells or occasional lymphocytes. In these sections, again the special stains already noted failed to demonstrate the presence of organisms or parasites.

No evidence of neoplasm was found on autopsy examination, although the air studies seemed to demonstrate such a condition. The granulomatous tissue discovered in the posterior third ventricle and scattered in the lateral ventricles over the ependymal surfaces and extending out around the pineal gland may explain these findings. It is to be presumed that this infection was present prior to surgical intervention and that the inflammatory reaction is similar to that seen in the occipital lobe. It is possible that no additional infection was introduced by the operative procedures and ventricular drainage subsequently instituted. Repeated cultures of the tissue and of the cerebrospinal fluid failed, except on one occasion which may be questioned, to demonstrate any organism. Extensive post mortem attempts to identify causal organism failed and numerous observers were unable to find any evidence of the etiologic agent involved, on studying the tissues removed. It would seem that the increased intracranial pressure may have been associated both with obstruction from the inflammatory changes in the upper brain stem and third ventricle and from cerebral swelling or edema, associated with the extensive infection, particularly noted in the regions of the ventricular system and the brain stem.

Clinical Diagnosis

Infiltrating neoplasm posterior third ventricle.

Anterior ventriculostomy and Torkildsen procedure bilaterally.

Dr. Salzer's Diagnosis

Pinealoma.

Anatomical Diagnosis

Granulomatous encephalitis with generalized ependymitis and basilar meningitis, of undetermined etiology.

Cerebral edema.

Bilateral post-operative Torkildsen procedure and anterior ventriculostomy.

Postoperative infection of wounds.

Generalized congestion of viscera.

Dr. Milton Rosenbaum: Two things bother me. First, did she have spinal punctures before the operative procedure, and, secondly, were sugars done on the cerebrospinal fluid? In an 11-year-old colored girl with stiffness of the neck, tuberculous meningitis should be considered.

Dr. Charles D. Aring: There were no cerebrospinal fluid studies before the operation.

Dr. Rosenbaum: What if she had had cells in the cerebrospinal fluid before the operative procedure?

Dr. Aring: Were there many plasma cells in the reaction about the aqueduct?

Dr. Murton Shaver: Yes, but they may be found in other disesase besides tuberculosis.

Dr. Aring: Unfortunately, cerebrospinal fluid serology was never performed in this case. Two blood Kahns were negative. The reasons for presenting this case are evident; even though pineloma is more common in this location, there are other lesions that result in these symptoms, and, as Doctor Rosenbaum suggests, diagnosis may have been more accurate had the cerebrospinal fluid been thoroughly exploited. This is a mistake that is made too frequently in a large institution of this sort. I believe, along with Doctors Rosenbaum and Shaver, that we could come closer to an etiologic diagnosis here with chemical and serological studies than with bacteriologic and neurohistologic studies.

Dr. Salzer: Weren't any of these estimations done on the first ventricular fluid?

Dr. Aring: A very thorough survey of the chart and a search through the laboratory data reveals no cell count, no chemical studies, and no serological studies on the cerebrospinal fluid.

An interesting point is the clearing of cells in the cerebrospinal fluid with penicillin therapy. This would suggest that the lesion, whatever it may have been, was amenable to antibiotic therapy which might be taken to mean that it was syphilitic or tuberculous and not parasitic. These are hints, but I don't think we may draw any conclusion from them.

Dr. Daniel Osher: This case brings to mind others. In one patient, tissue was obtained from the right frontal lobe at operation which was histopathologically considered by several examiners to be inflammatory reaction. Later on in the course of the illness, another operation established the fact that this was an ectopic pineoloma. I am not convinced that the lesion in this case is not a pineoloma. Sometimes peculiar changes take place in tumors with roentgen therapy, especially in pineoloma where there are large cells and small cells. A pineoloma can extend along the ependyma or along subependymal planes and give a picture similar to this one.

In cases similar to this in which obstructive hydrocephalus exists and posterior fossa operations are done, multiple nodular lesions are sometimes found. I recall one such biopsy read as tubercu-

loma which was eventually determined to be torulosis.

Dr. Miller: I would like to say a word in regard to Doctor Salzer's comments on radiotherapy. I believe he contradicted himself somewhat. First, he said that this patient's therapy was a gesture. He then quoted Horrax's work, saying that 12 cases were treated by roentgenotherapy alone. In the same report Horrax noted that 8 of these were living and well for from 2 to 15 years. Horrax noted that radiotherapy is the treatment of choice and should be done prior to attempts at surgical removal, and, if necessary, a decompression be done prior to roentgen therapy.

This patient's therapy was probably inadequate. Horrax advises rather low dosages. Kerr of the University of Iowa recommends at least 5,000 roentgens tumor dose.

Dr. Osher: Is there separation of the sutures in the films?

Dr. Miller: There may be some.

Dr. J. Park Biehl: What about the floor of the third portion of the right lateral ventricle?

Dr. Miller: Evaluation of the third portion of the lateral ventricles with asymmetrical filling is hazardous. I do not think that there will be significant variation in these structures pathologically.

Dr. Biehl: What is the possibility of the granuloma being on the basis of a postoperative wound infection?

Dr. Shaver: The postoperative wound infections were isolated and limited to the occipital area.

REFERENCES

1. Harris, W., and Cairns, H.: Diagnosis and treatment of pineal tumors. *Lancet,* Vol. I, 3-9, 1932.
2. Horrax, G.: Diagnosis and treatment of pineal tumors. *Radiol.* 52: 186-192, 1949.

50 Beds **THE RETREAT, Inc.** **Est. 1905**
DES MOINES 12, IOWA
For the diagnosis and treatment of Nervous and Mental Disorders in a homelike environment.
OCCUPATIONAL THERAPY, PHYSIOTHERAPY and SHOCK THERAPY
HERBERT C. MERILLAT, M.D., Medical Director
SYDNEY L. MACMULLEN, Superintendent

FENWICK SANITARIUM
Founded 1892 by the late Dr. Frank Fenwick Young
COVINGTON, LOUISIANA
For the Nervous Patient and the Addiction Diseases
ROY CARL YOUNG, M.D., *Medical Director* A. LAURIE YOUNG, *Manager*

GLENSIDE
JAMAICA PLAIN, BOSTON 30, MASS.
A small, attractively located sanitarium for nervous, mild mental or chronic illnesses.
MABEL D. ORDWAY, M.D.
6 Parley Vale Tel. Jamaica 0044

Sedation and Euphoria for Nervous, Irritable Patients
VALERIANETS-DISPERT®
Each tablet contains Ext. of Valerian 0.05 gm. dispergentized for maximum efficiency. Odorless and tasteless. Non-habituating. ACTION AND USES: A mild central nervous system depressent. For use in emotional upsets, anxiety states, nervous insomnia, the nervous syndrome of the menopause and of arteriosclerotic subjects.
1 or 2 tablets as required or 3 on retiring. Bottles of 50, 100 & 500.
STANDARD PHARMACEUTICAL CO., INC. 1123 Broadway, New York

Postgraduate Course In Clinical Neurology

University of Michigan Medical School
Department of Postgraduate Medicine

ANN ARBOR, MICHIGAN
May 5, 6 and 7, 1952

The course is designed to re-orient the practicing physician in regard to the nervous system and the disease aprocesses affecting it, stressing principally the close relationship between systemic disease in general and nervous system involvement or complications. The procedure of the neurologic examination will be reviewed with special emphasis on some of the newer diagnostic procedures. Many of the nervous system manifestations more commonly met with in general practice will be discussed individually. Diagnostic procedures, differential diagnosis and the newer modes of therapeutic approach will be presented. The course will be augmented by clinical presentations and a review of the essential laboratory procedures.

Detailed program may be obtained from

HOWARD H. CUMMINGS, M.D., Chairman
DEPARTMENT OF POSTGRADUATE MEDICINE
UNIVERSITY HOSPITAL ANN ARBOR, MICHIGAN

Costeff Sanitarium

Nervous and Mental Disorders

Shock Therapy (Insulin, Metrazol, Electroshock)

Home Environment

•

HARRY COSTEFF, M.D.
Psychiatrist

•

1109 N. Madison Avenue — Peoria 3, Illinois

Telephone — 4-0156

Therapy for Vascular Headache to Reverse the Physiologic Disturbance

Headache, a problem encountered in all kinds of medical practice, may occur in association with any of a variety of disorders, some organic, other purely functional.

Among the several types, functional headaches present the greatest problem because of their obscure etiology and recurrent nature.

Among these are:

Migraine (both classical and variant forms)
Tension headache
Psychogenic headache
Histaminic cephalgia

Wolff and his co-workers established that the pain of these headches is due to disturbance of the tonus of cranial blood vessels — hence the term *vascular headaches.*

The craniovascular changes associated with the several phases of the typical migraine attack are:

Vasoconstriction — to which the visual prodromata are attributable. It is possible to abort the attack during this phase in all but a few cases. (See treatment below.)

Vasodilatation — as the vessels lose their tone, exaggerated pulsations set in, resulting in the throbbing pain which characterizes vascular headache. Treatment for the attack is still effective during this phase. (See below.)

Vessel Edema — if the vasodilation continues for too long, vessel walls become edematous; this changes the character of the pain to a steady, intense aching. The attack can now no longer be checked, even with maximum dosage of specific drugs. *Moreover, sustained headache often induces reflex neck muscle tension, a source of residual pain.*

Therapy: 1. Reduce the frequency of attacks — psychotherapy and regulation of living habits to avoid fatigue and nervous tension.

2. Relieve the acute attack — of the numerous drugs which have been tried, ergotamine and its derivative preparations have proved most effective. The newest product is oral tablets of Cafergot®, N. N. R. (ergotamine with caffeine 'Sandoz'). When dosage is adjusted to the needs of the individual, Cafergot will give good relief in 85% of cases. It enables a greater number of patients to benefit from early administration since the oral route simplifies treatment as compared to parenteral therapy.

The dosage procedure is:

1. Take 2 tablets at first sign of the attack.
2. If attack continues, take one additional tablet every ½ hour until attack is terminated *(max. 6 tabs. per attack).*

Many migraine patients delay taking medication until the attack is at its height. Explicit dosage instructions may be forgotten unless the patient comes to realize their importance. Therefore, to encourage adherence to correct procedure, we have prepared pads outlining detailed dosage instructions. Supplies of these INSTRUCTION SLIPS will gladly be sent upon request.

GENERAL REFERENCES: DeJong, R.: Chicago M. Soc. Bull. 54: 106, 1951. Friedman, A.: Modern Headache Therapy. St. Louis, C. V. Mosby Co., 1951. Wolff, H.: Headache and Other Head Pain, N. Y., Oxford Univ. Press. 1948.

Sandoz Pharmaceuticals
DIVISION OF SANDOZ CHEMICAL WORKS, INC.
68 CHARLTON STREET, NEW YORK 14, N. Y.